Cornell University

Graduate School of Medical Sciences 1989 • 1990

Academic Calendar 1989–90

1989

Orientation for new students	Wednesday and Thursday, August 30 and 31
Opening Exercises	Wednesday, August 30
Registration for Quarter I* and Fall semester**	Thursday, August 31–Friday, September 1
Labor Day Holiday	Monday, September 4
Quarter I and Fall semester begin	Tuesday, September 5
Quarter I ends	Friday, October 27
Examinations for Quarter I	Friday, October 27–Friday, November 3
Registration for Quarter II*	Friday, November 3 and Monday, November 6
Quarter II begins	Monday, November 6
Thanksgiving recess	Thursday and Friday, November 23 and 24
Winter recess: Instruction suspended 5:00 p.m.	Friday, December 15

1990

Winter recess: Instruction resumed 9:00 a.m.	Tuesday, January 2
Last day for completing requirements for January degrees	Friday, January 12
Martin Luther King, Jr.'s Birthday observed	Monday, January 15
Quarter II and Fall semester end	Wednesday, January 17
Conferral of January degrees	Wednesday, January 17
Examinations for Quarter II	Thursday, January 18–Friday, January 26
Registration for Quarter III* and Spring semester***	Friday and Monday, January 26 and 29
Quarter III and Spring semester begin	Monday, January 29
Washington's Birthday observed	Monday, February 19
Quarter III ends	Friday, March 23
Examinations for Quarter III	Monday, March 26–Friday, March 30
Spring recess	Monday, April 2–Friday, April 6
Registration for Quarter IV	Friday, April 6 and Monday, April 9
Quarter IV begins	Monday, April 9
Tenth Annual Vincent duVigneaud Memorial Research Symposium; no classes	Tuesday, May 1
Last day for completing requirements for May degrees	Monday, May 14
Commencement Day, conferral of May degrees	Tuesday, May 22
Memorial Day Holiday observed	Monday, May 28
Quarter IV and Spring semester end	Friday, June 1
Examinations for Quarter IV	Monday, June 4–Friday, June 8

Summer Term 1990

Registration for summer research	Monday, June 25
Summer research term begins	Monday, June 25
Summer research term ends	Friday, August 17
Last day for completing requirements for August degrees	Friday, August 24
Conferral of August degrees	Monday, August 27

*for students enrolling in courses.

**for students conducting research only, who are on leave of absence, or are in absentia.

***for students changing from course work to research, who are going on leave of absence, or who are converting to in absentia status.

Note: Courses are taught on a quarterly basis, degrees are granted at ends of the Fall and Spring semesters and of the summer term. The dates shown in the calendar are subject to change at any time by official action of Cornell University.

In enacting this calendar, the Graduate School of Medical Sciences has scheduled classes on religious holidays. It is the intent of the school that students missing classes due to the observance of religious holidays be given ample opportunity to make up work.

Cornell University

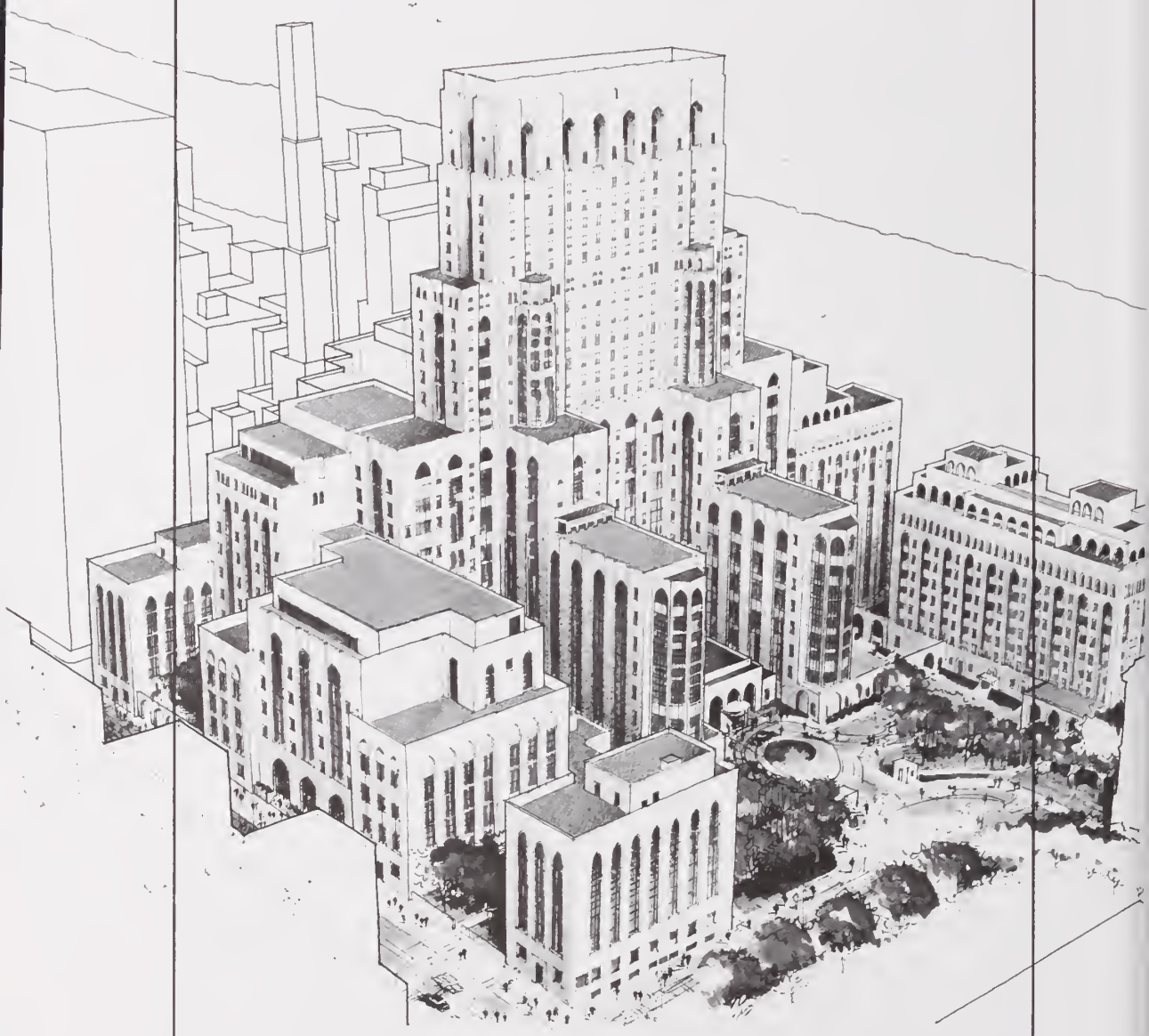
Graduate School of Medical Sciences 1989 • 1990

1300 York Avenue, Room A-139
New York, NY 10021
212, 746-6565

Contents

The courses and curricula described in this Catalog, and the teaching personnel listed herein, are as of July 1, 1989 and are subject to change at any time by official action of Cornell University.

New York Hospital–Cornell Medical Center



Cornell University
Graduate School of Medical Sciences

Purpose

The Graduate School of Medical Sciences, a semi-autonomous component of the Graduate School of Cornell University, provides opportunities for advanced study and research training in specific areas of the biomedical sciences. Graduate programs leading to the degree of Doctor of Philosophy are offered in biochemistry, cell biology and genetics, immunology, molecular biology, neuroscience, pharmacology, and in physiology and biophysics. Certain of these fields of study also offer programs leading to the degree of Master of Science. Collaborative programs with Cornell University Medical College lead to the combined degrees of Doctor of Philosophy and Doctor of Medicine.

The faculty of the Graduate School of Medical Sciences recommends the award of advanced general degrees not only as the result of the fulfillment of certain formal academic requirements, but also as evidence of the development and possession of a critical and creative ability in science. Demonstration of this ability is embodied in a dissertation which the candidate presents to the faculty as an original research contribution in the chosen area of study.

A close working relationship between student and faculty is essential to the program of the Cornell University Graduate School of Medical Sciences. Guidance for each student is provided by a Special Committee, a group of at least three faculty members selected by the student. This Special Committee is granted extraordinary independence in working with its student. Other than a broad framework of Graduate School of Medical Sciences requirements for residence, examinations, and a thesis, and additional requirements of the particular field of study chosen by the student, the Special Committee is free to design an individualized program of study with its students. No overall course, credit-hour, or grade requirements are set by the Graduate School of Medical Sciences. A student is recommended for a degree whenever the Special Committee judges the student qualified.

History

The opportunity for graduate study leading to advanced general degrees in the biomedical sciences was first offered at the Cornell University Medical College, in cooperation with the Graduate School of Cornell University, in 1912. In June of 1950, Cornell University, in association with the Sloan-Kettering Institute for Cancer Research, established additional opportunities for graduate study by forming the Sloan-Kettering Division of the Medical College. The resulting expansion of both graduate faculty and research training opportunities on the New York City Campus prompted the organization in January 1952 of the Graduate School of Medical Sciences, composed of two cooperative but separate divisions, known as the Medical College Division and the Sloan-Kettering Division. The Graduate School of Medical Sciences was given full responsibility for advanced general degrees granted for study in residence on the New York City campus of Cornell University.

Facilities

The Cornell University Graduate School of Medical Sciences is part of a large biomedical center extending along York Avenue between 65th and 72nd Streets on Manhattan's East Side. This complex includes Cornell University Medical College, New York Hospital, the Memorial Sloan-Kettering Cancer Center, and The Rockefeller University. The core facilities of the Graduate School of Medical Sciences, which include the research laboratories of its faculty, are located within the Cornell Medical College—New York Hospital complex and the Howard, Kettering, Rockefeller, and Schwartz Laboratory buildings of the Sloan-Kettering Institute for Cancer Research. Other buildings in this area provide student housing and recreational facilities. Several dining rooms and snack bars are located in this complex, and the immediate neighborhood abounds in a large variety of restaurants.

Especially noteworthy are two large biomedical libraries available to graduate students. The smaller of the two, the Medical Library—Nathan Cummings Center, contains over 27,000 books and journals. The Samuel J. Wood Library has a collection of 144,200 volumes and subscriptions to 1,700 journals. It is one of the country's first fully automated medical libraries featuring computer terminals which provide access to library materials and permit bibliographic searches in a number of data bases. A microcomputer center, with an extensive software collection, is maintained at the library for staff and students.

Organization

The faculty of the Graduate School of Medical Sciences is composed of the professional staffs of the basic science and clinical departments of Cornell University Medical College, and of those professional staff members of the Sloan-Kettering Institute for Cancer Research who hold faculty appointments.

Graduate training is offered in several areas of the biomedical sciences. These Programs of Study bring together faculty members who have related research and teaching interests.

Executive Committee

The Executive Committee is both the administrative and judicial board of the Graduate School of Medical Sciences and its members have continuing responsibility for the academic affairs of the school. The Committee is composed of the Chairpersons of the graduate programs, the Dean and Associate Dean, the Provost for Medical Affairs of Cornell University, the Director of the Sloan-Kettering Division, the Chairperson and Vice-Chairperson of the Faculty Advisory Committee (see below), and two non-voting, elected student representatives.

The Executive Committee considers such matters involving the interests and policies of the Graduate School of Medical Sciences as are referred to it by the Faculty Advisory Committee, by individual members of the Faculty, or are generated upon its own initiative. The Committee approves the addition or deletion of fields of study, reviews the admission of students, approves a student's major and minor fields, reviews the curriculum and requirements for degrees.

The Executive Committee is chaired by the Dean, who is the academic administrative officer of the Graduate School of Medical Sciences and is also an Associate Dean of the Graduate School of Cornell University. The Associate Dean, who is also an Assistant Dean of the Graduate School of Cornell University, is the Secretary of the Executive Committee.

Faculty Advisory Committee

The Faculty Advisory Committee is the primary body representing the views of the Faculty of the Graduate School of Medical Sciences. The Committee advises the Dean and the Executive Committee on the impact of educational and policy matters under their consideration and recommends changes in educational activities, procedures, and policy of the Graduate School of Medical Sciences.

The Faculty Advisory Committee is composed of elected faculty representatives from the graduate programs and one elected student representative from each Division. The Chairperson and Vice-Chairperson of the Committee are elected by its membership. Non-voting members are the Dean and Associate Dean, the Provost for Medical Affairs of Cornell University, and the Director of the Sloan-Kettering Division.

Special Programs

Medical Scientist Training Program (M.D.-Ph.D.)

This program is designed to expose a student to both medical and graduate disciplines during a six-year course of study. The combination of skills in basic research and experience in a clinical setting will prepare graduates from this program to pursue investigative careers in the biomedical sciences or in clinical medicine. The student spends the first two years as a medical student studying the basic medical sciences and attending regular graduate seminars. The summer months are spent in the laboratory learning experimental techniques and doing research. The third, fourth, and fifth years of the student's program are spent as a full-time graduate student and are devoted mainly to laboratory research and writing the thesis. The sixth year of the program is devoted to clinical clerkships. This six-year program represents the minimum time required to satisfy residence requirements of both the M.D. and Ph.D. degrees at Cornell University. Successful applicants to the program will become M.D.-Ph.D. fellows and will receive a full tuition scholarship and a stipend covering living expenses for the six-year period.

In this program, preclinical and clinical training leading to the M.D. degree are provided by the faculty and in the facilities of Cornell University Medical College. Special features have been introduced into the medical-school curriculum to reflect the training objectives of the M.D.-Ph.D. program. Graduate training in research leading to the Ph.D. degree is provided under the auspices of the Cornell University Graduate School of Medical Sciences in the laboratories of faculty members located both in the Medical College and at the Sloan-Kettering Institute.

For application to the M.D.-Ph.D. program, see p. 59.

Ph.D.-M.D. Program

Students enrolled in the Graduate School of Medical Sciences may be eligible for admission into the Ph.D.-M.D. Program, jointly sponsored by the Medical College and the Graduate School of Medical Sciences. This program is designed for those graduate students who find that their teaching and research goals require the acquisition of the M.D. degree in addition to the Ph.D. degree. The program is *not* designed as an alternate path for students who have the M.D. degree as their primary goal, but who have not been accepted by a medical school. Those who know, at the time of application to Cornell, that they want to pursue a course of study leading to both degrees should apply to the M.D.-Ph.D. program described above.

See p. 60 for application and graduation requirements of the Ph.D.-M.D. program.

Faculty and Research Activities

Biochemistry

Faculty

Mary E. Anderson
John P. Blass
Adele I. Boskey
Esther M. Breslow
Arthur J. L. Cooper
Gordon F. Fairclough
Jerald D. Gass
Jack Goldstein
Owen W. Griffith
David P. Hajjar
Rudy H. Haschemeyer
Bernard L. Horecker
Chun-Yen Lai
Alton Meister
Ursula Muller-Eberhard
Abraham Novogrodsky
Julian R. Rachele (Emeritus)
Hugh D. Robertson
Albert L. Rubin
Edward T. Schubert
Richard I. Soffer
Kurt H. Stenzel
Suresh S. Tate
Sidney Udenfriend
Daniel Wellner
Kenneth R. Woods
David Zakim

Research Activities

Members of the Biochemistry program are engaged in research spanning a wide spectrum of scientific areas. Thus, the research in *Dr. Meister*'s laboratory is concerned with the study of enzymes, especially those involved in amino acid, peptide, and protein metabolism. It involves the isolation of enzymes, the determination of their structure and properties, and the use of techniques such as isolation of mRNA and cDNA. The research is basic in nature, but significant relationships between this research and human disease have been discovered and are also being explored. Current work involves the metabolism and function of glutathione, including the relationships of this tripeptide to transport, metabolism, radiation, and chemotherapy.

Dr. Anderson's research involves the synthesis of compounds, based on enzymological studies, which decrease or increase glutathione levels in mammalian cells. These compounds are used *in vitro, in vivo,* or in culture to study the metabolism and function of glutathione. Enzyme studies also include protein sequencing, cloning and site-specific mutagenesis. Recent research interests include the mechanisms of development of multi-drug resistance.

Dr. Boskey's research is concerned with elucidating the factors controlling physiologic and dystrophic calcification. Hydroxyapatite formation and growth are studied in solution, in collagen gels, in animal tissues, and in cell culture. Recent studies have concentrated on the mechanism of action of proteoglycans (a mineralization inhibitor) and acidic phospholipids (promoters of mineralization). Studies are also in progress on: the role of vitamin D metabolites in bone lipid metabolism, the actions of matrix proteins in the regulation of calcification, and the effect of trace elements on bone metabolism.

Dr. Breslow is concerned with understanding the forces that determine the specificity of protein-protein interactions and the relationship between protein structure

Views of Manhattan from Cornell Medical College.

and function. She has been studying the interactions of the pituitary peptide hormones, oxytocin and vasopressin, with their storage protein, neurophysin. These studies are directed towards elucidating the binding site regions of the hormones and of the protein and at quantitating the energies of different components of the interaction. A second area of research concerns the mechanism by which proteins are degraded intracellularly during normal protein turnover. The aims of these studies are to understand the precise role of ubiquitin, a small protein known to be involved in this process, and to elucidate the mechanisms underlying the selection of proteins for degradation.

Dr. Cooper's laboratory is working in the area of α-keto acid biochemistry and pyridoxal phosphate enzymes. Another area of active research is the metabolism of amino acids and ammonia in the brain and other tissues. For this purpose, molecules labeled with short-lived positron-emitting isotopes are synthesized and their distribution in tissues is analyzed by various techniques including positron emission tomography. Cerebral energy metabolism, with particular emphasis on the malate-aspartate shuttle and its disruption in various disease states are also being investigated.

Dr. Goldstein is studying the structure and function and erythrocyte surface antigens and is working on enzymatic methods for the removal of immuno-dominant sugars responsible for blood group A and B activity. He is also isolating and characterizing proteins exhibiting Rh structures, clarification of the genetic systems involved in Rh expression and modification of such antigenic sites by chemical and enzymatic procedures.

Dr. Griffith's research involves the design, synthesis and utilization *in vivo* of enzyme-selective inhibitors and substrates. These compounds are used both to evaluate and to control the metabolite flux through various pathways in intact animals. Recent studies have focused on the manipulation of glutathione and cysteine metabolism. Enzyme-selective inhibitors were developed that allow both glutathione biosynthesis and utilization to be blocked; techniques allowing extracellular cystine formation to be controlled were also developed. The inhibitors were shown to be useful in treating animal trypanosomiasis, enhancing oxidative killing of tumor cells, and preventing the formation of leukotriene C. New inhibitors are now being developed to allow *in vivo* control of carnitine metabolism. Applications of these compounds include the investigation and therapy of inherited diseases of lipid metabolism and diabetes.

Dr. Hajjar's laboratory has focused on cell-cell and cell-virus interactions during the pathogenesis of arteriosclerosis. Studies are aimed at elucidating the cellular mechanisms by which viruses and chemical mutagens alter gene expression that would modify the structural state of arterial lipid in such a manner as to render immobilized lipid.Techniques used in the laboratory include transcriptional and translational assays to define gene regulation during arterial injury, and differential scanning calorimetry and mass spectroscopy to characterize the physical state of the arterial lipids.

Dr. Haschemeyer's laboratory concentrates on the development of physical methods to study molecular structure and interactions. Current emphasis is directed toward computer modeling of biological flow methods and heterogeneous-phase reactions. Additional computer applications are directed toward defining prognostic factors and treatment protocols that optimize graft survival in kidney transplant patients.

Dr. Horecker is working on the isolation and characterization of peptides from the thymus gland and evaluation of their possible function as regulators of cellular im-

munity. The cloning of the genes for prothymosin α and parathymosin and identification of promoter and enhancer sequences are major current objectives.

Dr. Lai's research is concerned with the structure and function of biologically active proteins. Work from his laboratory has shown that subunit A1 of cholera toxin is fully responsible for the toxin's ability to stimulate adenylate cyclase in mammalian cells. Isolated subunit A1 was also shown to catalyze an efficient transfer of the ADP-ribose moiety from NAD to a membrane protein. Structural studies revealed the presence of a characteristic conformation for the NAD-binding site in the A1 subunit. In another project, evidence has been obtained for a two-domain structure of the angiotensin converting enzyme: the hydrophobic carboxy-terminal portion of the enzyme is anchored to the cell membrane and the amino-terminal half, with the active site, is exposed to the blood circulation. Structural analyses indicate that the lung and testis enzymes may be the products of two distinct genes, and experiments are in progress to explain the close similarities between the two enzymes.

Dr. Muller-Eberhard is investigating the mechanisms of transport of iron protoporphyrin IX and its metabolic precursors by proteins in the blood stream as well as within hepatocytes. She is studying the exchange of porphyrins between proteins purified from serum and from hepatocytes; developing methods which delineate the function of these proteins in the delivery of porphyrins to hepatocytes and their intracellular distribution; and assessing the interaction of these proteins with artificial and biological membranes to learn how they may facilitate ligand transport across cellular and intracellular barriers.

Dr. Robertson's work involves the structure and function of biologically important RNA molecules. Recent work has focused on RNA-catalyzed cleavage of viroid-like RNA pathogens during their replication. For example, a region of the genomic RNA of the delta hepatitis agent has been isolated and found to contain a highly active RNA enzyme ("ribozyme") region. Work on RNA processing and replication of viroid-like agents and their replication by rolling circle mechanisms, and a 2-domain model for the structure of the delta hepatitis RNA genome, structural probe for RNA tertiary structure at or near biologically active sites involving ultraviolet light-induced cross-linking and mapping by direct techniques of the resulting new covalent linkages.

The main objective of *Dr. Soffer*'s research is to characterize the physical, chemical, and biochemical properties of angiotensin II receptor which has been purified to a nearly homogeneous state from rabbit hepatic membranes.

Drs. Stenzel and Novogrodsky are interested in determining mechanisms involved in the regression of metastatic kidney tumor mediated by autologous killer cells activated by the oxidizing mitogens and recombinant interleukin 2 (rIL2). They are using *in vitro* systems to determine mechanisms of cell mediated cytotoxicity. These investigations include an analysis of mononuclear cell sub-populations involved, mechanisms of target cell lysis (membrane structures vs. soluble factors), target specificity, and synergistic effects of additional biologic response modifiers. *In vivo* systems are used to determine mechanisms of tumor lysis *in vivo* mediated by administration of activated killer cells and rIL2 in mouse tumor models. Clinical studies are underway in patients with metastatic renal cell carcinoma to determine efficacy and toxicity of adoptive immunotherapy. Alterations in patients' immune responses are determined. These studies include a structural and functional analysis of circulating mononuclear cell populations.

Dr. Tate is investigating the mechanisms by which the kidney epithelial cell achieves its structural and functional polarity. Brush border membrane peptidases are

being used as models to study the synthesis, membrane integration, processing, and intracellular targeting of these membrane proteins employing techniques of classical protein chemistry, immunology, cellular and molecular biology. Other research involves characterization and regulation of expression of variant forms of a cell-surface glycoprotein in certain cancer cells.

Dr. Wellner's laboratory is concerned with the structure and function of enzymes involved in amino acid metabolism, such as L-amino acid oxidase and threonine deaminase. Techniques employed for the study of protein structure include amino acid analysis and microsequencing using a gas-phase protein sequencer.

Recent Publications

Anderson, M. E. (with A. Meister): Inhibition of γ-Glutamyl Transpeptidase and Induction of Glutathionemia by γ-Glutamyl Amino Acids, *Proc. Natl. Acad. Sci. U.S.*, 83, 5029–5032 (1986).

Anderson, M. E. (with R. K. Singhal and A. Meister), Glutathione, A First Line of Defense Against Cadmium Toxicity, *FASEB J.*, 1, 220–223 (1987).

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Boskey, A. L., Hydroxyapatite formation in a dynamic gel system: Effects of Type I collagen, lipids, and proteoglycans, *J. Phys. Chem.* 93:1628–1633, 1989.

Boskey, A. L. (with Donnelly, R.), The effect of gallium on seeded hydroxyapatite growth, *Calcif. Tiss. Int.*, 44:138–142, 1989.

Breslow, E. (with Peyton, D. and Sardana, V.), Application of peptide-mediated ring current shifts to the study of neurophysin-peptide interactions: A partial model of the neurophysin-peptide complex. *Biochemistry* 26:1518–1525, 1987.

Breslow, E. (with Live, D. H., and Cowburn, D.), Binding of Oxytocin and 8-arginine-vasopressin to neurophysin studied by 15N NMR using magnetization transfer and indirect detection via protons, *Biochemistry* 26:6415–6422, 1987.

Breslow, E. (with Burman, S., Wellner, D., Chait, B., and Chaudhary, T.), Complete assignment of neurophysin disulfides indicates pairing in two separate domains, *Proc. Natl. Acad. Sci. U.S.A.*, 86:429–433, 1989.

Cooper, A. J. L. (with Nieves, E., Coleman, A. E., File-DeRicco, S., and Gelbard, A. S.), Short-term metabolic fate of [^{15}N] ammonia in rat liver *in vivo*. *J. Biol. Chem.* 262:1073–1080, 1987.

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Cooper, A. J. L. (with Lai, J. C. K.), Cerebral ammonia metabolism in normal and hyperammonemic rats, *Neurochem. Pathol.*, 6:67–95, 1987.

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Griffith, O. W. (with Weinstein, C. L.), Cysteinesulfonate and β-sulfopyruvate metabolism. Partitioning between decarboxylation, transamination, and reduction pathways, *J. Biol. Chem.*, 263:3735–3743, 1988.

Griffith, O. W. (with Weinstein, C. L., and Haschemeyer, R. H.), *In vivo* studies of cysteine metabolism. Use of D-cysteinesulfinate, a novel cysteinesulfinate decarboxylase inhibitor, to probe taurine and pyruvate synthesis, *J. Biol. Chem.*, 263:16,568–16,579, 1988.

Hajjar, D. P. (with Hajjar, K. A., and Nachman, R. L.), Tumor necrosis factor-mediated increase in PDGF gene expression in human endothelial cells, *J. Exp. Med.*, 166:235–245, 1987.

Hajjar, D. P. (with Nicholson, A. C., Hajjar, K. A., Sando, G. N., and Summers, B. D.), Decreased messenger RNA translation in herpes virus-infected arterial smooth muscle cells: Effects on cholesteryl ester hydrolase, *Proc. Natl. Acad. Sci. U.S.*, 86:3366–3370, 1989.

Horecker, B. L. (with Frangou-Lazaridis, M., Clinton, M., and Goodall, G. J.), Prothymosin α and parathymosin: Amino acid sequences deduced from the cloned rat spleen cDNAs, *Arch. Biochem. Biophys.*, 263:305–310, 1988.

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Meister, A. (with Larsson, A.), Glutathione synthetase deficiency and other disorders of the γ-glutamyl cycle, in: *The Metabolic Basis of Inherited Disease* (Scriver, C. R., et al, Eds.), 6th edition, Chapter 31, 1989.

Meister, A., Novel drugs that affect glutathione metabolism, in *Biochemical Modulation of Anticancer Agents: Experimental and Clinical Approaches* (F. A. Valeriote and L. H. Baker, Eds.), Martinus Nijhoff Publishing, Boston, pp. 245–276, 1988.

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Robertson, H. D. (with Branch, A. D., and Benenfeld, B. J.), Evidence for a single rolling circle in the replication of potato spindle tuber viroid, *Proc. Natl. Acad. Sci. U.S.*, 85:9128–9132, 1988.

Robertson, H. D. (with Nicholson, A. W., Niebling, K. R., and McOsker, P. L.), Accurate *in vitro* cleavage by RNase III of phosphorothioate-substituted RNA processing signals in bacteriophage T7 early mRNA, *Nucleic Acid Res.*, 16:1577–1591, 1988.

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Cell Biology and Genetics

Faculty

Rosemary F. Bachvarova
David M. Bader
J. Michael Bedford
June L. Biedler
Anthony M. C. Brown
Michael A. Caudy
Raju S. K. Chaganti
Moses V. Chao
Sandra Citi
Zbigniew Darzynkiewicz
Paul J. Deutsch
David B. Donner
Magdalena Eisinger
Donald A. Fischman
Leonard P. Freedman
James L. German, III
Marvin Gershengorn
David P. Hajjar
Eric A. Jaffe
Irwin Klein
Ione A. Kourides
Paul Marks
Joan Massague
Malcolm A. S. Moore
Ralph L. Nachman
Carl Nathan
Joel D. Pardee
Louis M. Pelus
Richard A. Rifkind
Enrique Rodriguez-Boulan
Anuradha D. Saad
Martin Sonenberg
Lisa Staiano-Coico
Paul Szabo
Martin Teintze
Paula Traktman
Doris A. Wall
Perrin C. White
David Zakim

Research Activities

The faculty of the Program in Cell Biology and Genetics conduct research in a broad range of fields which include the most exciting areas of genetics and cell, developmental and molecular biology. Specific interests include the developmental biology of the early embryo and of cardiovascular and muscle tissues; membrane biology; cell motility and the cytoskeleton; the molecular biology of cell growth, differentiation and oncogenic transformation; endocrinology and hormone receptors; human somatic cell and cyto-genetics; molecular virology. These studies are pursued using the most current cell biological, genetic, molecular and immunological methodologies in modern and well-equipped facilities.

Dr. Bachvarova is interested in gene expression during early mammalian development. The following areas are being investigated: control of translation of endogenous and injected mRNAs during meiotic maturation of mouse oocytes, the role of small RNAs in this process, and the expression of genes with a possible regulatory role in pre- and early postimplantation embryos. *Dr. Bader*'s laboratory is concerned with the development of the heart. Specific interests are the differential expression of myosin heavy chains in the developing myocardium, and the mechanisms by which myocardial heterogeneity are generated. Monoclonal antibody and recombinant DNA technologies provide the basis for these studies of cardiac myogenesis *in vivo* and *in vitro*. Processes in both the male and female reproductive systems which contribute

to conception are the focus of research in *Dr. Bedford*'s laboratory. The cellular events undergone by spermatozoa during their maturation in the epididymis are under study; in the female, research is directed toward understanding sperm capacitation, sperm transport to the site of fertilization, and to the mechanism of fertilization. *Dr. Biedler*'s research concerns the genetic mechanisms underlying the cellular acquisition of multiple resistances to cancer chemotherapeutic agents. At least two amplified genes with a role in this process have been identified and are being studied. A second area of research is the cell biology of human neuroblastoma. This system, too, involves amplification of a specific gene and consequent cytogenetic abnormalities. Current studies are focused on the correlation of the differential expression of the N-myc oncogene and the EGF receptor gene with varying states of malignant transformation and/or cell differentiation.

Dr. Brown is studying the molecular mechanisms of oncogene action, concentrating on tumors induced by the mouse mammary tumor virus (MMTV). A major focus of his research is the function of the proto-oncogene *int*-1, which is activated by MMTV in mammary tumors and is also implicated in early embryonic development of the nervous system. *Dr. Caudy,* who will join the program in January, 1990, is interested in developmental neurobiology. The research in his laboratory will focus on the *Drosophila* gene *daughterless* which plays an essential role in the formation of peripheral neurons and in sex determination. The major aim of *Dr. Chaganti*'s research is to define the role played by hereditary factors in the etiology and progression of human malignancy. Studies focus on inherited changes associated with cancer predisposition and with acquired changes associated with various tumors. Chromosomal rearrangement, gene amplification, point mutation and gene deregulation are considered. *Dr. Chao*'s research interests focus on gene expression and regulation in mammalian cells. Molecular genetic techniques are being applied to the gene for the nerve growth factor receptor and the role of the receptor in the mechanism of action of NGF and in the development of the nervous system.

The focus of *Dr. Citi*'s research is a newly identified component of tight junctions, cingulin. Structural and functional analyses of the purified protein and the gene will be undertaken. The development of cytochemical, biophysical, and molecular probes and techniques for the analysis of normal and tumor cells is the focus of *Dr. Darzynkiewicz*'s efforts. These probes may aid in cancer diagnosis, classification, and therapeutic evaluation. Mechanistic studies on the pharmacological action of DNA intercalating agents on tumor cells are also being undertaken. *Dr. Deutsch*'s laboratory studies the mechanisms whereby classic hormones and neurohormones induce gene expression via cAMP-responsive and phorbol ester-responsive DNA motifs. The regulation of gonadotropin-alpha gene expression in placental cells is a current focus of research. *Dr. Donner* is studying the molecular basis for signal transduction through peptide hormone and cytokine receptors. A major focus of present research is the structure, function and regulation of the receptor for tumor necrosis factor.

The identification and characterization of factors involved in growth stimulation or differentiation of skin melanocytes and keratinocytes *in vitro,* and the effect of cells grown in tissue culture and growth factors on wound healing *in vivo,* is the focus of *Dr. Eisinger*'s work. *Dr. Fischman*'s research focuses on the cell and molecular biology of sarcomere assembly in developing skeletal and cardiac muscle. Monoclonal antibody and recombinant DNA technologies, as well as electron microscopy and fluorescence energy transfer, are being applied to the study of post-translation steps involved in myofibrillogenesis. *Dr. Freedman,* who will join the program in the fall of

1989, is interested in analyzing the mechanisms by which DNA binding proteins modulate differential gene expression. His work is centered on the study of proteins containing the important zinc finger motif. Several aspects of human genetics are under study in *Dr. German*'s laboratory, including disturbances of malformation, disturbances of sexual development, and human cancer. Somatic cell genetic, cytogenetic, and molecular genetic approaches are being used.

The focus of research in *Dr. Gershengorn*'s laboratory is the delineation of the mechanisms of signal transduction used by extracellular regulatory molecules. In particular, the inositol lipid-calcium-protein kinase C pathway which mediates the actions of thyrotropin-releasing hormone (TRH) in cells of the anterior pituitary gland is under study. Research is directed towards defining the molecular details of the interactions of the TRH-receptor, G protein and the effector enzyme (a phospholipase C) and the formation of a TRH-responsive pool of inositol lipids. Research in *Dr. Hajjar*'s laboratory concerns the interactions between the smooth muscle cells and endothelial cells within the lining of blood vessels. The goal is to understand the perturbations of this endothelium which accompany and exacerbate cholesterol accumulation during the formation of atherosclerotic plaque, and to determine the role which Herpes viruses infection may play in this process. *Dr. Jaffe*'s interest is in the response of endothelial cells to exogenous stimuli; current research includes study of the interaction of thrombin and other physiological agonists with endothelial cell surface proteins and the resultant induction of prostaglandin production. Cytokine-induced expression of cell surface antigens is also being studied.

Dr. Klein is studying the effects of cardiac contractility and thyroid hormone on the regulation of cardiac myosin synthesis. Hormonal regulation of gene expression is the focus of *Dr. Kourides*' research. Of major interest to *Drs. Marks and Rifkind* are the cellular and molecular mechanisms that control coordinated gene expression and proliferation during induced cell differentiation. The principal experimental model is the murine erythroleukemia cell (MELC), which is a virally transformed red blood cell precursor arrested at a stage of the lineage called the colony-forming cell for erythropoiesis. A number of defined chemical agents can induce MELC to express the genetic program of erythroid differentiation. Present studies address the signal mechanisms triggered by inducing agents, the mechanism of induced gene expression, and the identification and cloning of genes implicated in the programmed cessation of cell proliferation.

Dr. Massague's research interests concern the mediation of intercellular communication by growth and differentiation factors. Much of the research is centered on understanding the activities of transformation growth factor-β (TGF-β). The focus of work in *Dr. Nachman*'s laboratory is the biochemistry of platelet membranes and the macromolecular assembly of adhesive proteins on various cell surfaces and in the extracellular matrix. The structure and function of endothelial cell membranes is also under study. *Dr. Nathan*'s efforts are aimed at understanding how phagocytic leukocytes kill microbes, tumor cells, and normal host elements at inflammatory sites. Investigations into the biochemical bases of cytotoxicity by macrophages and granulocytes are integrated into a context of cell biology and clinical investigation. *Dr. Pardee*'s research is concerned with the regulation of the actin cytoskeleton by actin-binding proteins. Regulatory proteins, such as myosin, severin and an actin filament bundling factor, have been isolated and are being analyzed for their roles in cell migration and neoplastic transformation.

Along with *Dr. Moore, Dr. Pelus*'s primary interest concerns the regulation of hematopoiesis; the roles of prostaglandin E, TNF, IL-1 and other cell-derived regulators

of this process are currently under investigation. A primary focus of Dr. Pelus's laboratory is the delineation of the roles of hematopoietic growth factors in *in vivo* animal models. In this context, a novel inhibitory pathway has been identified *in vivo* which may have significant effects in protecting hematopoiesis from the effects of chemotherapy. *Dr. Rodriguez-Boulan*'s main interest is an understanding of the cellular and molecular mechanisms that regulate the traffic and targeting of membrane proteins in eucaryotic cells, with an emphasis on the polarized distribution of apical and basolateral plasma membrane proteins in epithelial cells. The experimental approaches utilized include cell and molecular biology, virology, immunology and electrophysiology. The assembly and stability of the contractile apparatus of skeletal muscles are the primary interests of *Dr. Saad*'s laboratory. The primary approach is the use of biochemical and biophysical assays to examine the mechanism by which individual contractile proteins are inserted into and removed from fully functional myofibers.

Dr. Sonenberg's long-range objective is the molecular description of membrane transduction of peptide hormonal messages after interaction with a specific membrane receptor or other membrane component. *Dr. Staiano-Coico*'s research involves the investigation of epidermal cell maturation and differentiation in culture in conjunction with preclinical and clinical studies on the usefulness of epidermal cell sheets as transplantable grafts. The use of flow cytometry in the detection of individuals at high risk for the development of colorectal cancer is also being examined. *Dr. Szabo*'s laboratory is investigating the molecular basis of cellular senescence, specifically concentrating on those genes which are normally expressed during the GO quiescent stage of the cell cycle but whose dysregulation may lead to senescence. Also under study is the molecular genetics of age-related disorders such as Alzheimer's disease in humans. At present, *Dr. Teintze*'s research is focused on two areas: the mechanism by which membrane proteins insert into the lipid bilayer, using model membrane systems, and the mechanism by which certain proteins are sorted to specific membranes within eukaryotic cells.

The main focus of *Dr. Traktman*'s research is a molecular genetic analysis of vaccinia virus. Of particular interest are the temporal regulation of gene expression and the coordination of viral DNA replication. A variety of molecular, genetic and biochemical techniques are being employed to identify and characterize the viral genes and enzymes involved in DNA replication, homologous recombination, and the maintenance of DNA topology. *Dr. Wall*'s laboratory conducts research in membrane biology, with an emphasis on receptor-mediated endocytosis and an analysis of intracellular membrane systems. The *Xenopus* oocyte is being used as a model cell to study the pathways of ligands and receptors during endocytosis, and the establishment and maintenance of distinct membrane systems during oogenesis and early embryonic development. The major projects in *Dr. White*'s laboratory concern the relationships between structure and function of cytochrome P-450 enzymes, in particular the mechanisms by which mutations in genes encoding such enzymes cause human disease. The primary focus is on inherited defects of steroid metabolism. The main interests of *Dr. Zakim*'s laboratory are interactions, within the plane of a membrane, between lipids and enzymes and between lipids and small hydrophobic substances. A major emphasis is on how the physical and chemical properties of the lipids regulate the function of integral membrane proteins.

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Immunology

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Research Activities

The main interests of the Immunology faculty are focused on the complex molecular and cellular mechanisms responsible for the development and regulation of the immune system. Research programs can be grouped into three main areas: (1) immunogenetics of cell surface molecules involved in the differentiation and function of normal and malignant lymphoid cells; (2) cellular immunology of the interactions between cells and their secreted products, and (3) tumor immunology of the transformed tumor cell and its host, aimed at designing possible diagnostic and therapeutic strategies. Research in all three areas involves studies using both animal models and human cells. Immunology is multidisciplinary in its approaches and has generated its own methodology (such as the production of monoclonal antibodies, and the continuous *in vitro* growth and cloning of lymphoid cells), in addition to using the methods of other disciplines, including biochemistry and molecular biology. For example, the analysis of the biological significance of a given lymphoid cell surface antigen is not only studied using classical genetics and in functional assays using monoclonal antibodies, but also by isolating the molecule and defining its structure using biochemical techniques and characterizing its gene with the tools of molecular biology. Thus, the general approach of the research program is to define immunological events at the biological, biochemical and molecular levels.

In the field of tumor immunology, *Dr. Albino*'s laboratory is examining the role of specific oncogenes in the pathogenesis of malignant melanoma and renal carcinoma. This includes a comprehensive study of the steps required for the transformation of human melanocytes and proxymal tubule cells. In addition, this laboratory also studies the structure and function of melanoma cell-surface differentiation proteins and their gene sequences.

Dr. Becker's current research interests concern the effects of tobacco constituents on the immune system and related mediator pathways and how these may contribute to the pathogenesis of cardiovascular and pulmonary disease.

Dr. Chiorazzi's laboratory is investigating the mechanisms and cellular interactions involved in B lymphocyte activation and differentiation to antibody secreting cells. Studies of selected lymphoid cell surface receptors and their ligands are integral components of these analyses. Monoclonal populations of lymphoid cells, derived by either Epstein-Barr virus transformation or somatic cell hybridization, are frequently employed in this approach. Structural and functional studies of antibodies produced in certain autoimmune disorders have provided basic clues to the relationship between normal and disease states. Autoimmune and allergic disorders as well as the chronic lymphoid malignancies are this laboratory's clinical interests.

The central themes for *Dr. Dupont*'s laboratory are the characterization of the genetic composition of the genes of the human major histocompatibility complex (MHC); the investigation of the molecular genetic basis for the expression of these extensive genetic polymorphisms of the MHC-encoded cell surface antigens as detected in the population; and the biological role of MHC gene products in immunoregulation and other biological functions. The laboratory is also involved in investigations in the area of transplantation immunology, particularly in relation to the understanding of mechanisms responsible for graft vs. host disease.

Investigations in *Dr. Flomenberg*'s laboratory focus primarily on the activation and effector functions of human lymphocytes. A large portion of this work concerns the molecular interactions between the T cell and its target, focusing on the major histocompatibility complex gene products that initially activate or serve as targets for T cells, as well as the T cell surface molecules that are important for T cell function. Additional studies of autoreactive T cells, and the molecular genetics of lymphocyte differentiation are in progress.

For the mouse, the majority of genes encoding lymphocyte antigens are organized in distinct multigene families positioned on several chromosomes. Study of these gene clusters continues to be the major theme of *Dr. Hämmerling*'s efforts. The immunogenetics of murine and human lymphoid and hemopoietic cell surface antigens using monoclonal antibodies is another area of Dr. Hämmerling's studies, with special emphasis on their role in T cell activation.

Dr. Houghton's research program is investigating the expression and regulation of antigens by human tumor cells. Genes coding for these antigens are being identified, sequenced and expressed. The role of differentiation and malignant transformation in the expression of these antigens is an area of active study. Antigens on tumor cells that are potential targets for recognition by the immune system are of particular interest.

Dr. Knowles' laboratory has developed monoclonal antibodies that provide an extensive panel of unique probes to examine cell surface molecules and their functional epitopes. These have been used in the biochemical and genetic characterization of the human histocompatibility antigens and the differentiation antigens of the human T cell, B cell and NK cell lineages. Defective expression of HLA class II genes and recombination events within the class II region are also being investigated at the genomic level.

The molecular genetics of the human major histocompatibility complex or HLA genes is the major area of study of *Dr. Lee*'s laboratory. Her goals are to identify and characterize genes and their products that govern the tissue specific expression of

class II genes. These studies involve the analysis of defects in expression of mutant cell lines derived from immunodeficiency patients. In addition, the laboratory is investigating regulatory polymorphisms associated with different alleles.

Investigations of the glycoproteins and glycolipids of human tumor cells and normal cells are the focus of research in *Dr. Lloyd*'s laboratory. Particular emphasis has been placed on the biochemical identification and characterization of these components.

Dr. Murray has several inter-related research interests. These include (1) macrophage activation for antimicrobial activity, (2) intracellular infections caused by *Toxoplasma gondii* and *Leishmania donovani,* (3) interferon-gamma, and (4) the AIDS T cell defect.

Dr. Nathan's efforts are aimed at understanding how phagocytic leukocytes kill microbes, tumor cells, and normal host elements at inflammatory sites. Investigations into the biochemical bases of cytoxicity by macrophages and granulocytes are integrated into a context of cell biology and clinical investigation.

Dr. Novogrodsky's research interests include mechanisms of lymphocyte activation, oxidative mitogenesis and effector mechanisms mediated by mononuclear cells and cytokines. Current work involves the mitogenic properties of hemin and its analogs and other iron-containing agents (the ferro-mitogens), and the evaluation of their immune stimulatory and anti-tumor activity.

The main effort in *Dr. Oettgen*'s laboratory is on the serological analysis of human cancer antigens, the humoral and cellular immune responses to human cancer, and the development and application of human cancer therapies using immunogenic cancer vaccines, monoclonal antibodies, and cytokines.

Dr. Old's research is concerned with the development of two new approaches to cancer therapy: tumor necrosis factor (TNF) and monoclonal antibodies directed against surface determinants on malignant cells. The latter is part of a general effort to analyze the cell surface of human and murine tumors, with the aim to characterize the important surface molecules, mostly with monoclonal antibodies and other serological procedures.

The principal objective of *Dr. O'Reilly*'s Bone Marrow Transplantation Program is the development and improvement of transplantation approaches for the treatment of lethal disorders of the blood system through an integrated program of clinical and basic research in immunology, hematology, genetics, and transplantation biology.

Dr. Posnett's laboratory is interested in basic problems of immunology. The approach is primarily molecular. The topics under study include the human T cell antigen receptor and several lymphocyte membrane molecules that may serve as lymphokine receptors. In the former case he is interested in understanding the process of antigen/MHC recognition by T cells. Studies are focusing on T cell antigen receptor V gene usage and its relationship with antigen/MHC reactivity. Also of interest are disease associations with the T cell antigen receptor genes. He is also cloning the genes of several putative lymphokine receptors. These studies are aimed at understanding the function of these membrane activation antigens.

The main objective of *Dr. Rettig*'s research is to define the rules and molecular mechanisms by which intrinsic genetic differentiation programs, extrinsic differentiation signals, and malignant transformation are integrated in specific cell types to generate the complex cell-surface patterns seen in human tumors.

Dr. Rothermel's laboratory is investigating the induction of cytokines by the intracellular bacteria of the genus *Chlamydia.* Current work focuses on the requirements

for induction of interleukins 1 and 2 and gamma interferon, and the role of interleukin 1 in the pathogenesis of chlamydial disease.

Dr. Russo's research is concerned with the role of MHC molecules in the regulation of the immune response. Two major areas are under investigation: (1) the dual function of MHC class II molecules in the induction of self-tolerance and in the biology of the autoreactive T-cell network, (2) the relationship between selective loss of MHC class I molecules by tumor cells and tumor progression.

Dr. Siskind is concerned with factors regulating the immune response. In particular, he is studying (1) the role of idiotype anti-idiotype interactions in determining clonal expression and (2) the role of T cells bearing receptors for the Fc of IgD in regulating the magnitude of the immune response.

Dr. Stenzel's studies have focused on biochemical mechanisms of lymphocyte activation, transplantation immunology and the role of cell mediated cytotoxicity in the control of cancer growth. The latter studies include both basic and clinical investigation of adoptive immunotherapy in renal adenocarcinoma.

Dr. Stutman's research is focused in two areas: (1) the ontogeny, maintenance and involution of functional T cells, including T cell subsets and the role of the thymus proper in such processes, and (2) the immunological components of the tumor-host interaction, especially the production of cytotoxic effector cells which can kill tumor cells by production of tumor necrosis factor (TNF) and other lytic molecules.

Dr. Weksler's research concerns two areas: (1) The biology of autoreactive T lymphocytes and (2) the immunobiology of aging. The former studies are aimed at understanding the development and regulation of the immune system; the latter at understanding the biological processes that lead to the diseases of aging.

Dr. Yang's laboratory is conducting studies of the molecular mechanisms controlling class I MHC gene expression during cellular differentiation and neoplastic transformation, as well as the biological role of class I MHC determinants in tissue transplantation. Another area of study is the activation and differentiation of T-lymphocytes and characterization of T-lymphocyte differentiation antigens and their function.

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Molecular Biology

Faculty

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Anthony Brown
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Dale Dorsett
Erik Falck-Pedersen
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Research Activities

The faculty of the Graduate Program in Molecular Biology offers graduate research training in a variety of systems on problems related to the replication, transcription, translation and function of genetic information in developing organisms and differentiating cells. The research activities of the faculty can be divided into four broad areas of study: DNA replication and recombination; regulation of RNA synthesis and processing; receptors and their role in cell function and differentiation; and retroviruses, proto-oncogenes, and development.

DNA Replication and Recombination

DNA replication in prokaryotes is under study in the laboratories of *Dr. Marians* and *Dr. O'Donnell.* Dr. Marians focuses on studies of the enzymological mechanisms of DNA replication in *Escherichia coli,* using cell-free systems. The use of *in vitro* DNA replication systems composed of purified replication proteins enables detailed analyses of the interaction of the replication proteins with each other and with the DNA template. The role of topology in DNA replication, as well as the mechanisms of DNA topoisomerases, is also under study in his lab. A detailed examination of the molecular mechanics of DNA replication is also the focus of *Dr. O'Donnell*'s laboratory. The dynamic motions on templates of the multi-protein replicative polymerase of *E. coli* and its interaction with other proteins at the replication fork are under study. Dr. O'Donnell is also beginning to investigate the control of initiation of replication of Epstein-Barr virus.

Faculty investigating eukaryotic DNA replication employ several different viral systems. *Dr. Berns* uses the life cycle of the human adeno-associated virus AAV2 to model how gene expression and DNA replication are regulated. *Dr. Hurwitz*'s laboratory uses the adeno and SV40 viral DNA replication systems as probes for the enzymatic mechanisms of cellular DNA replication. The regulation of bovine papilloma virus DNA replication is studied by *Dr. Lusky* using molecular genetics to define and characterize the viral genes required for replication *in vivo* and using biochemical approaches to study BPV DNA replication *in vitro*. The replication of AAV, adenovirus, SV40, and BPV require host cellular proteins, thus these viral systems also allow these investigators to study the endogenous mechanisms for DNA replication in mammalian cells.

Both *Dr. Traktman*'s and *Dr. Rabkin*'s laboratory study the replication of large DNA viruses that encode their own DNA replication machinery. Dr. Traktman employs both biochemical and molecular genetical techniques to define the genes of vaccinia virus that are required for its replication. Dr. Rabkin is developing an *in vitro* system for the replication of herpes simplex viral DNA in order to identify and characterize the proteins involved in these processes.

The molecular processes controlling the structure, function, and genetic properties of chromosomes are being studied by the laboratories of *Drs. Lustig* and *Hackett*. Using molecular genetics and biochemistry, *Dr. Lustig* is investigating the mechanisms that have evolved for replicating telomeres, the unique ends of chromosomes required for stability, and role these sequences play in chromosome segregation and recombination.

Dr. Hackett is also interested in the structure of the bacterial genome and how it changes over time. His immediate objective is to construct detailed restriction maps of the genomes of several related isolates of *Halobacterium halobium*. Comparisons will reveal how genome structure evolves both normally and in response to selective pressure.

Another key cellular process that occurs on DNA is the exchange of genetic information through the process of recombination. *Dr. Holloman*'s laboratory studies the genes and the enzymes involved in this complicated process. Model studies focus on the mechanism of synapsis and DNA strand exchange.

Regulation of RNA Synthesis and Processing

Many aspects of the regulation of gene transcription and RNA processing are under active investigation by members of the Molecular Biology Program. These include the definition of controlling DNA and RNA sequences, the identification and characterization of the proteins and enzymes involved, and the elucidation of the mechanisms that dictate temporal and spatial patterns of gene expression.

Using genetic and molecular genetic techniques, *Dr. Osley* is investigating the basis of the periodic expression of the histone genes in yeast.

Research in *Dr. Sheffery*'s laboratory is directed at understanding how proteins and DNA interact to form structures that influence gene transcription, using the mouse globin genes as a model. Particular effort is devoted to understanding tissue-specific gene expression.

In a related effort, the basis of sequence-specific recognition of DNA by proteins is studied by *Dr. Barany* using a combination of molecular biology, X-ray crystallography, and NMR spectroscopy.

Dr. Krug's research focuses on the unique interaction of influenza virus with its host cell as a model system for elucidating control mechanisms involved in the synthesis, processing, and translation of both viral and cellular messenger RNAs. *Dr. Falck-Pedersen* is characterizing the regulatory elements involved in eukaryotic transcription termination and RNA processing using genetically reconstructed adeno-virus as a model vector. Both biochemical and genetic aspects of transcriptional control, with particular emphasis on transcription termination in purified *in vitro* systems, are under study by *Dr. Shuman* using vaccinia virus as a model.

Dr. Dorsett's laboratory is using both genetic and molecular genetic techniques to define the *cis*- and *trans*-acting factors that regulate virus-like transposons in *Drosophila.* These transposons are responsible for a number of naturally occurring mutations in *Drosophila* and have been shown to affect the expression of the mutated host genes at the level of transcription.

Dr. Hurwitz's group studies the enzymes and enzymological processes involved in mRNA splicing in human cells.

Receptors and Their Role in Cell Function and Differentiation

Several laboratories are investigating receptors that transmit signals to the interior of the cell after forming a complex with a specific ligand.

Elucidation of the mechanism of action of insulin and related growth factors, leading to a detailed understanding of the receptor molecule as well as the mechanism(s) by which it transmits signals from the cell surface to its interior is the principal goal of *Dr. Rosen*'s research.

In a series of experiments in *Dr. Ravetch*'s laboratory, the molecular genetic analysis of cell surface receptor proteins is being conducted, aimed at defining their modulation, mechanism of signal transduction, and developmental regulation by isolation and characterization of genes that code for proteins binding immunoglobulins (FC receptors), by studying the interaction of the malaria producing parasite with the erythrocyte, and by characterizing the activated macrophage phenotype.

Dr. Neff is interested in the role of vacuolar-type proton ATPasesin endocytosis and vacular functions in *Saccharomyces cerevisiae.* Toward this goal two genes have been cloned that have identity with proton ATPase subunits, one of which codes for a proton channel protein.

The gene for human nerve growth factor receptor has been isolated by *Dr. Chao*'s laboratory. Recombinant DNA technology is being used to study the important structural features of the gene, the molecular basis of differential receptor expression during development, and the mechanism of signal transduction.

Using the generation of transgenic mice as the major experimental tool, *Dr. Lacy* is studying the regulation and function of the CD4 and CD8 cell surface glycoproteins during T-cell maturation in the thymus. CD4 and CD8, respectively, recognize and bind to nonpolymorphic regions on class II and class I major histocompatibility complex (MHC) proteins; their interactions with the MHC proteins are believed to regulate the signals transduced by the T-cell receptor during T-cell development.

Retroviruses, Proto-oncogenes, and Development

The research activities of the Molecular Biology faculty in this area are quite diverse and include studies on retroviral vectors, retroviral induced neoplastic diseases, the

role of proto-oncogenes in cell and tissue differentiation, embryonic axis formation and the development of the nervous system in *Drosophila,* and gene function in the early mouse embryo.

Efficient methods to introduce genes into human cells, using retroviruses, are being developed in *Dr. Gilboa*'s laboratory. These methods are used to develop an efficient gene therapy protocol for the treatment of genetic disorders and to modify and amplify specific immune responses in the human patient.

The major objective of *Dr. Hayward*'s laboratory is the elucidation of the molecular basis of the induction of neoplastic disease, using avian leukosis viruses as model systems. Of particular interest at the present time is the identification and characterization of oncogenes involved in late stages of tumor progression.

The current research goal in *Dr. Besmer*'s laboratory is to understand the function of the proto-oncogene c-*kit,* a transmembrane receptor kinase; the c-*kit* ligand is being sought and molecular aspects of c-*kit* mediated signal transmission are being investigated in hemotopoietic cell differentiation and development.

Dr. Brown is studying molecular mechanisms of oncogene action, concentrating on tumors induced by the mouse mammary tumor virus (MMTV). A major focus of his research is the function of the proto-oncogene *int*-1, which is activated by MMTV in mammary tumors and is also implicated in early embryonic development of the nervous system.

Drs. DeLotto, Jack, and Ballinger use *Drosophila* as an experimental organism for the study of development and cell determination. *Dr. DeLotto* studies the biochemical mechanisms underlying embryonic axis formation using genetic and molecular biological approaches. *Dr. Jack* is currently investigating the molecular genetics of development of the peripheral nervous system. *Dr. Ballinger*'s laboratory is investigating mechanisms of differentiation, pattern formation and behavior in the *Drosophila* visual system with a combination of molecular and genetic techniques. Photoreceptor neurons are the subject of studies focused on a terminal differentiation antigen, and on the mechanism of pattern formation. To investigate the function of complex neural processing networks, behavioral mutations that alter the processing of visual information are under study.

Dr. Lacy's group is working on identifying and isolating genes that are required for early mouse development by generating insertional mutations in the germ line of transgenic mice.

Recent Publications

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Neuroscience

Faculty

Chiye Aoki
Harriet D. Baker
Ira Black
Dana C. Brooks
Arthur Cooper
E. DiCicco-Bloom
Cheryl Dreyfus
Marian J. Evinger
Daniel Gardner
James Gibbs
Gary Gibson
Steven A. Goldman
Bernice Grafstein
Katherine Halmi
Lorraine Iacovitti
Tong Joh
Roger Lasken
David Levy
Mary P. Meeley
Teresa A. Milner
Michiko Okamoto
Gavril Pasternak
Virginia Pickel
Fred Plum
William Pulsinelli
Don Reis
D. A. Ruggiero
Jeri A. Sechzer
Gerard P. Smith
Peter E. Stokes
Gladys Teitelman
E. Townes-Anderson
Jonathan Victor
Robert Young

Research Activities

Dr. Aoki studies the cellular basis for interaction between extrathalamic afferents and intrinsic neurons in the neocortex using light and electron microscopic immunocytochemistry. One project is focused on examining synaptic and non-synaptic contacts between cholinergic and noradrenergic axon terminals and of intracortical neurons containing GABA and peptides. Another project examines the preciseness of the localization of beta-adrenergic receptors in relation to catecholaminergic terminals using electron microscopic immunocytochemistry.

Dr. Harriet Baker studies the factors underlying the determination and maintenance of neuronal phenotype. Using the olfactory system as a model, the research focus is on neurotransmitter expression during development and aging as well as in response to deafferenting lesions. Immunocytochemical, neurochemical, molecular biological and neuronal tracing techniques are utilized in these studies.

Dr. Ira B. Black studies the molecular genetics underlying neuronal plasticity in the peripheral nervous system and the brain. A combination of *in vivo,* tissue culture, molecular biological, biochemical and morphological techniques are employed to explore plasticity, and its role in the function of the nervous system. Developmental as well as aging models are being studied.

Dr. Dane C. Brooks is using signal averaging techniques to study the manner in which auditory information is processed as it passes through the first relay nucleus of the auditory system in the cat. The potential fields generated by the subdivisions of this nuclear complex are being mapped using an IBM XT and computer graphics programs.

Dr. Arthur J. L. Cooper is working in the area of 2-oxo acid biochemistry and pyridoxal phosphate enzymes. Another area of active research is the metabolism of ammonia, neurotransmitter amino acids and other amino acids in the brain. For this purpose, molecules labeled with short-lived radioisotopes are synthesized and used as tracers for metabolic studies. Cerebral energy metabolism, with particular emphasis on the malate-asparate shuttle, and its disruption in various disease states is also being investigated.

Dr. DiCicco-Bloom studies molecular regulation of neuronal proliferation in the peripheral nervous system and the brain. A combination of *in vivo,* tissue culture, biochemical and morphologic techniques are employed to specifically identify neurons and define extracellular signals and intracellular second messenger mechanisms governing neuronal mitosis. The relationships between neuronal cell division, a developmentally restricted event, and differentiation are being examined.

Dr. Cheryl Dreyfus' research examines phenotypic development of specific neurons of the central nervous system and emphasizes definition of environmental factors which may influence brain cell development. This work has concentrated on ontogeny of noradrenergic neurons of the locus coeruleus, as well as dopaminergic cells of the substantia nigra and peptidergic and cholinergic neurons of the striatum and nucleus basalis.

Dr. Marian Evinger's research interests focus on transcriptional regulation of neurotransmitter gene expression. Molecular biological approaches are employed to study neural and hormonal regulation of mRNA encoding catecholamine synthesizing enzymes *in vivo* and *in vitro.*

Dr. Daniel Gardner studies how neurons use chemical synaptic transmission to communicate with one another. Neurons in ganglia of the mollusc *Aplysia* are probed by intracellular recording, voltage clamping, patch clamping, and computer-based analysis to yield principles of organization of cell networks. One project focuses on properties of transmitter-activated channels which are altered to produce different postsynaptic currents. A second project combines neurophysiology with artificial intelligence techniques to ask how neuronal biophysics coordinates the activity of neurons in a network.

Dr. James Gibbs' research focuses on the neurobiology of motivated behaviors, especially the neuroendocrine mechanisms controlling feeding behavior in animals and the pathophysiology of eating disorders in humans.

Dr. Gary E. Gibson examines the relation of calcium, oxidative metabolism and neurotransmitters to altered mental function and cell death. These interactions are examined in animal models of conditions that alter mental function in man (aging, hypoxia, and thiamin deficiency) as well as in tissues from Alzheimer patients. *In vivo* neurotransmitter metabolism is related to behavior and to molecular mechanisms *in vitro.* Human studies include enzyme measurements on autopsied brain as well as studies of calcium dynamics in lymphocytes, red blood cells and cultured skin fibroblasts.

Dr. Goldman is interested in neuroplasticity in the adult brain. His research is focused upon the molecular mechanisms subserving neural production, migration and differentiation in a neurogenic region of the adult songbird brain. These cellular events are examined both *in vivo* and *in vitro,* with the aim of determining the regulatory constraints on neurogenesis and neuroblastic migration in the adult CNS.

Dr. Bernice Grafstein is concerned with problems of nerve regeneration and the response of nerve cells to injury. Techniques used include light and electron micros-

copy and radioactive isotope methods for analyzing the axonal transport of proteins and other cellular constituents.

Dr. Katherine Halmi's current research on anorexia nervosa and bulimia nervosa includes long term follow-up studies, investigation of appetite and satiety mechanisms in eating disorder patients, assessing taste preferences, neuroendocrine investigations and psychological assessments.

Dr. Lorraine Iacovitti's current research activities are directed toward the study of the developing nervous system. She is currently examining the principles which govern phenotypic expression of particular neurotransmitters in neurons of the peripheral and central nervous system.

Dr. Tong H. Joh's main interest is to study the biochemistry and molecular genetics of neurotransmitter enzymes and receptors, and neurospecific protein. Multidisciplinary studies with molecular biologists, developmental biologists, and histochemists include the structural analyses of genes coding for neurotransmitter enzymes, gene regulation at the transcriptional level, quantitative analysis of mRNAs and gene expression during development and aging.

Dr. Roger Lasken is studying the control of neuronal development. A biochemical approach is taken in analyzing the regulation of neurotransmitter synthesis within the context of cellular differentiation. Methods of protein purification and tissue culture are being employed in the isolation of regulatory factors.

Dr. David E. Levy is developing techniques for predicting which comatose patients will recover and which will not. These efforts include utilization of positron emission tomographic scanning to study unconscious patients. He collects detailed clinical information on patients with stroke so that methods for predicting recovery from stroke can be developed as they have been for coma. Development of an easily-utilized data entry and analysis system designed to accept serial clinical data on patients with a variety of neurological illnesses is an integral part of these efforts. He is also investigating effects of thrombolytic therapy in patients with acute stroke.

Dr. Mary P. Meeley is interested in neurochemical regulation of synaptic transmission. The model system currently studied is brainstem pathways controlling arterial pressure and heart rate. The focus is on elucidation of specific transmitters involved in mediating autonomic signals within principle nuclei, and their possible interactions, and on isolating and identifying new putative transmitters, e.g. a clonidine-like substance in the brain, the putative endogenous ligand interacting with imidazole receptors in the ventrolateral brainstem. Methods of purification of small molecules and specific assay systems are developed.

Dr. Teresa A. Milner studies the ultrastructural basis for transmitter interactions in (1) the septo-hippocampal pathway involved in learning and memory; and (2) brainstem and spinal cord nuclei associated with cardiovascular regulation. Both studies utilize either dual labeling immunocytochemical techniques or immunocytochemical methods combined with tract-tracing techniques at the electron microscopic level of analysis. The major transmitters of interest include catecholamines, acetylcholine, opioids, and somatostatin.

Dr. Michiko Okamoto investigates pharmacologic and neuropharmacologic bases of the tolerance and dependence produced by general CNS depressants. Barbiturates, alcohol and benzodiazepines are the prototypes for the study. Synaptic dysfunctions in neonates born under the influence of these drugs will also be investigated.

Dr. Gavril W. Pasternak is studying the molecular pharmacology of centrally active analgesics. Work in the laboratory currently is focused upon the biochemical and

pharmacological characterization of the various opiate receptor subtypes. One goal of the laboratory includes examining membrane-bound and affinity-purified receptors and their potential coupling with effector systems. Another is the correlation of the various subtypes with specific opiate actions *in vivo*. Finally, the anatomical localization of these sites within the central nervous system is studied with quantitative autoradiography. Many of these approaches have utilized a series of opiate affinity labels developed within the laboratory.

Dr. Virginia M. Pickel uses immunocytochemical methods to examine (1) the synaptic interactions between transmitter-specific neurons in selective brain circuits of normal adult animals, and (2) structural alterations in identified populations of neurons during normal development and following lesions and drug treatment. These questions are being systematically addressed for mesolimbic and nigrostriatal dopaminergic circuits implicated respectively in neuropsychiatric and movement disorders. Additional research using similar approaches is directed toward cardiovascular vagal reflexes involving catecholaminergic neurons in the dorsal medulla.

Dr. Fred Plum, Chairman of the Department of Neurology, focuses his research efforts on cerebral metabolism in disease states and the identification of cellular-subcellular mechanisms responsible for ischemic cell death.

Dr. William Pulsinelli studies the molecular mechanisms of ischemic injury to brain neurons and glia. Techniques used in these studies include *in vivo* and *in vitro* (tissue culture) models of ischemic injury to brain cells, radioisotopic measurements of cerebral blood flow and glucose metabolism, fluorometric measurements of high energy organic metabolites, analysis of phosphorylation of brain proteins, and light and electron microscopic studies of cell injury.

Dr. Donald J. Reis' research interests are the central neural and neurochemical mechanisms governing control of the autonomic nervous system, cerebral blood flow and metabolism. His research also includes mechanisms governing the death of brain neurons in response to aging and injury.

Dr. D. A. Ruggiero's interests include: anatomical and neurochemical pathways in brain which maintain normal resting levels of arterial blood pressure; neural substrates of the baroreceptor reflex; pathways underlying the cerebellar regulation of autonomic activities and cerebral blood flow; areas of autonomic representation in cerebral cortex and brainstem reticular formation; adrenaline synthesizing neurons, their pathways in the central nervous system; their role in cardiopulmonary regulation; and afferent (pain) neurotransmission.

Dr. Jeri A. Sechzer's research interests include: early development, behavioral toxicology, neural mechanisms of memory and learning, and neurosensory perception. Her current activities include: (1) The effect of lithium chloride on maternal behavior and early development; (2) Olfactory and gustatory perception in depression; (3) Bioethical issues concerning the use of animals in research and education.

Dr. Gerard P. Smith is interested in the behavioral neuroscience of eating and its disorders. Current experiments include the measurement of central monoamines during eating behavior, the role of gut peptides, such as cholecystokinin, to stop eating, animal models of eating disorders using genetic and sham feeding rats, and the experimental analysis of taste and eating in human patients with various types of eating disorders.

Dr. Peter E. Stokes is interested in neuroendocrine function in affective disease. Measurements of hypothalamic-pituitary-adrenocortical (HPA) function at various levels of this axis are obtained in patients with depression vs healthy normal controls

and patients with other psychiatric diagnoses. Current specific interests include: response of the HPA system to administration of CRF, ACTH, dexamethasone and adrenocortical steroid blockers, pharmacokinetics of dexamethasone, measurement of multiple adrenal steroids, investigation of the relationship between HPA function and biogenic amine and sympathetic nervous system activity. A second area of interest is the investigation of lithium pharmacokinetics and the pharmacology-toxicology of lithium isotopes in animals and humans.

Dr. Gladys Teitelman's research interests include the cellular events controlling the expression of neurospecific proteins, such as neurotransmitter biosynthetic enzymes in autonomic ganglia of avian and mammalian embryos. Another area of her active research revolves around mechanisms involved in the differentiation of the endocrine cells of pancreatic islets from cells transiently expressing neurospecific enzymes. The techniques used in these studies include tissue culture, biochemistry and immunocytochemistry.

Dr. Townes-Anderson is interested in the cell biology of retinal neurons. Currently, cells isolated from the adult vertebrate retina are used *in vitro* to address questions concerning synaptic function and plasticity. Membrane recycling at the photoreceptor synapse is being examined with morphological techniques including rapid freezing and electron microscopy. Localization of neurotransmitter receptors is performed on isolated second and third order neurons. And regeneration of functional synapses is being investigated in cultures of adult nerve cells.

Dr. Jonathan D. Victor studies visual processing at retinal and cortical levels. Research techniques include single-unit recording, evoked potentials, psychophysics, and mathematical modelling. Other research interests include novel approaches to nonlinear systems analysis and signal processing as applied to neural systems.

Dr. Robert C. Young's interest is in major affective illness developing in late life. Indices of brain neurotransmitter function and behaviors are studied in patients when symptomatic and after drug treatment and in normal subjects. The laboratory measures applied include catecholamine metabolite excretion, neuroendocrine tests, brain imaging, and antidepressant drug concentrations.

Recent Publications

Akoi, C., Milner, T. A., Sheu, K.-F. R., Blass, J. P., and Pickel, V. M., Regional distributions of astrocytes with intense immunoreactivity for glutamate dehydrogenase in rat brain: Implications for neuron-glia interactions in glutamate transmission. *J. Neurosci.* 7(7):2214–2231, 1987.

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Pharmacology

Faculty

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Francis M. Sirotnak
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Research Activities

Dr. Bertino is interested in the transfer of drug resistant genes into hematopoetic cells: Both electroporation and viral vectors have been studied as methods of introducing drug resistant genes (chloramphenicol-acetyl transferase; an altered dihydrofolate reductase from 3T6 cells) into mammalian cells in culture, and into bone marrow cells. This method appears to be a powerful one for introducing substances into cells that are ordinarily excluded, and thus study their intracellular activity. The aim is to produce long-term expression of drug resistant genes in hematopoetic stem cells. Both *in vitro* (CFU_c) and *in vivo* (CFU_s) studies are being pursued in mice. The purpose of these studies is to produce drug resistance of marrow stem cells, thus allowing larger doses of the desired drug to be utilized for therapy.

Site specific mutagenesis of the dihydrofolate reductase gene: By using oligonucleotides with specific base changes, it has been possible to synthesize full-length cDNAs containing the desired mutation via the M-13 cloning system. The purpose of these studies is to better understand the effects of specific amino acid substitutions on substrate and inhibitor binding, and to hopefully develop an altered enzyme with a decreased affinity for methotrexate, but with good catalytic activity.

Development of a rapid *in vitro* test for detection of resistance to methotrexate and trimetrexate: Work has continued, utilizing leukemia cells from patients sensitive and resistant to methotrexate, to determine the degree and mechanism of drug resistance.

Studies with the new antifolate, trimetrexate: A phase 1 study has been completed. In rodent models, this drug was found to synergize with Carboxypeptidase G, a folate depleting enzyme, and when utilized following methotrexate treatment. Clinical studies are planned using these combinations.

Dr. Chan is interested in the functions and interactions of prostaglandins and neurohypophysial peptides in the kidney and the uterus. Current research covers investigative studies from subcellular levels to the whole organism. Certain analogs of oxytocin and vasopressin have been found to stimulate urinary sodium and water excretion. This renal effect of the peptide appears to be mediated by renal prostaglandin release. The biochemical mechanisms of this peptide-induced prostaglandin release is the principal concern of our research. Also studied are the renal activities of

peptide analogs specifically synthesized for the project with the aim to discover specific prostaglandin-releasing peptides that may be useful for the treatment of renal hypertension.

In the uterus, the roles of prostaglandins and oxytocin in the regulation of uterine contractions and termination of pregnancy are investigated. This research seeks an understanding of the mechanism of initiation of labor, especially relating to preterm labor. Oxytocin-receptor and gap-junction formations in myometrial cells are important biochemical and morphological markers in the initiation of labor. Accordingly, a study is made of the effects of prostaglandins and oxytocin on the density of oxytocin-receptors and on the formation of gap-junctions in myometrial cells. Highly potent oxytocin antagonists have been synthesized for this project and their application in the prevention of preterm labor in the pregnant rat model will be investigated. Also studied are the physiological roles of ovarian oxytocin and uterine prostaglandins in the function of the corpus luteum, as well as the potential of intervention of this ovarian-utero axis in the regulation of fertility or as causal factor in abortion.

Dr. Chou's major research objectives are the study of: (1) the mechanisms of action of antitumor and antiviral agents; (2) the biochemical and pharmacological bases for the selectivity of effects on different targets; and (3) the derivation of theoretical formulations for dose-effect relationships that permits the automated computer analysis of relative potency and therapeutic index and facilitates the study of the interaction of multiple drugs in combination chemotherapy. The compounds of current interest include potent antiherpes viral agents, anti-human immunodeficiency virus (anti-HIV) agents, classical antifolate analogs and lipid-soluble antifolates. Emphasized are pharmacodynamics, pharmacokinetics and preclinical toxicology, the determination of affinity and efficacy of drug interaction with enzymes or other targets, the elucidation of molecular events following the binding or incorporation of a drug into macromolecules, and the development of computer programs for drug evaluation, especially the synergism/antagonism of drugs in combinations. Currently several of the compounds mentioned above are in clinical trials. Also, software for dose-effect analysis has recently been developed for microcomputers.

Dr. Felsen is interested in the role of arachidonic acid metabolites (AAMs; prostaglandins, hydroxy acids and leukotrienes) and other mediators of inflammation (e.g., platelet-activating factor and monokines) in renal and urinary tract function. The role of these compounds both *in vivo* and *in vitro* is studied using a combination of techniques. These include measurement of renal blood flow, both isotopically and nonisotopically; glomerular filtration rate and other parameters of renal function (Na^+ and K^+ excretion, water excretion, etc.). *In vitro,* both isolated organs and cell culture techniques are used for studies of renal and urinary tract cells. These methods may provide an understanding of the molecular mechanisms involved in the interaction of AAMs and other inflammatory mediators in different models of renal and urinary tract disease.

Dr. Griffith's research involves the design, synthesis and utilization *in vivo* of enzyme selective inhibitors and substrates. These compounds are used both to evaluate and to control the metabolite flux through various pathways in intact animals. Recent studies have focused on the manipulation of glutathione and cysteine metabolism. Enzyme-selective inhibitors were developed that allow both glutathione biosynthesis and utilization to be blocked; techniques allowing extracellular cystine formation to be controlled were also developed. The inhibitors were shown to be useful in treat-

ing animal trypanosomiasis, enhancing oxidative killing of tumor cells, and preventing the formation of leukotriene C. In other studies, novel carnitine analogs were synthesized as inhibitors of carnitine palmitoyltransferase and were shown to block long-chain fatty acid oxidation *in vivo*. In mice with diabetes, a disorder characterized by underutilization of glucose and overutilization of fats, these compounds prevent ketoacidosis and restore normal blood glucose levels. Studies are continuing in which carnitine analogs are used to probe the regulatory interactions between carbohydrate and fatty acid metabolism.

Dr. Inturrisi's research activities are directed toward understanding the biochemical basis of the pharmacodynamic effects of opioids. In laboratory animals studies utilizing molecular probes are aimed at defining the factors that regulate opioid peptide gene expression, biosynthesis and release so as to establish the relationships between treatments that alter opioid peptides and their mRNAs and the functions (e.g., analgesia) of the endogenous opioid peptides. Clinical studies are aimed at developing pharmacokinetic-pharmacodynamic models from patient data that can be used to improve analgesic therapy and provide insight into the quantitative aspects of the development of tolerance to opioids in these patients. The ultimate goal of these studies is a more precise definition of the interrelationship between the exogenous and endogenous pain modulating systems.

Dr. Levi examines the possibility that mediators of inflammation and immune hypersensitivity cause cardiac dysfunction and play a role in the pathogenesis of sudden death, heart attacks, and cardiac failure. The molecular bases of the decrease in cardiac contractility by leukotrienes, platelet-activating factor and histamine, as well as the electrophysiological and biochemical effects of these mediators are being studied. Further, the relevance of complement activation and anaphylatoxin generation in cardiac hypersensitivity is being investigated. The possible physiological role of endogenous cardiac histamine as a modulator of the responses to activation of the sympathetic nervous system is being uncovered. The receptors mediating this histamine-induced modulation are being sought and the molecular mechanisms of this modulation are being assessed. The synthesis, release and actions of endothelium-derived relaxing factor/nitric oxide in the heart and vasculature are being investigated.

Dr. Mendelsohn's laboratory is studying the epidermal growth factor (EGF) receptor from three points of view. (1) We are investigating exogenous and endogenous agents controlling autophosphorylation of the receptor, including regulators of protein kinase C and activated receptors for other growth factors. Receptor trafficking and metabolism are being characterized, the role of receptor dimerization and high affinity binding are under exploration, and we are studying the physiologic role of receptor overexpression in malignancy. (2) We are exploring the interactions between endogenous factors (autocrine loops) and agents that promote or inhibit cell proliferation, the latter including TGF beta and the interferons. (3) Our group has produced anti-EGF receptor monoclonal antibodies which inhibit EGF/TGF alpha binding and block receptor activation. These are utilized in the above biologic experiments, and we are carrying out preclinical studies and Phase I clinical trials in patients, exploring the capacity of antireceptor antibodies to act as antitumor agents. Conjugates of antireceptor antibodies with cytotoxic agents and radionuclides are under investigation in human tumor xenograft model systems.

Dr. Okamoto studies the pharmacologic and neuropharmacologic bases of the

drug dependence caused by general central nervous system depressants in adults and neonates exposed to drugs during their fetal period. Barbiturates, benzodiazepines and alcohol are the prototype drugs for these studies.

Ongoing studies involve development of analytical procedures for the determination of sedative-hypnotic drugs and their pharmacologically active metabolites, steroids, biogenic amines, and polypeptides in biofluids; neuroelectrophysiologic and behavioral monitoring of acute and chronic drug actions, investigation of functional and cellular mechanisms for the chronic effects produced by these drugs.

Dr. Pasternak studies the biochemical and pharmacological properties of various subclasses of opiate receptors within the central nervous system. Molecular approaches include binding studies and affinity labeling of receptors using a series of irreversible opiate agonists and antagonists developed and synthesized in this laboratory. Computerized quantitative autoradiographic studies are aimed at the distribution of the various subtypes of receptors complement the biochemical studies. In addition to these molecular studies, the biochemically defined binding subtypes are correlated with specific opiate actions, including analgesia, respiratory depression, gastrointestinal motility and hormone modulation, using classical pharmacological techniques. Again, the selective affinity labels developed in this laboratory have proven invaluable in these studies.

Dr. Reidenberg pursues a fundamental question in clinical pharmacology, "Why do different people react differently to the same dose of the same medicine?" His program in clinical pharmacology addresses this question in several different ways. One way is to apply the tools of pharmacokinetics to learn if differences in drug disposition or tissue sensitivity are the reasons for differences in responses. Currently, this approach is being used to learn how aging modifies drug response so that drug therapy can be appropriately individualized for elderly people. This research is also attempting to differentiate effects of aging itself from the effects of diseases that progress as people age. A current focus is on the decline in kidney function with age and the ability of the kidney to "adapt" to modest levels of nephrotoxic chemicals in the environment.

Dr. Rifkind's interest in environmental toxicology has led to the investigation of the biochemical mechanisms of polychlorinated biphenyl and dioxin toxicity. Toxic polychlorinated biphenyls and dioxins are known to bind to a cytosolic receptor (Ah receptor) which controls the expression of a group of gene products, the major one being a form of cytochrome P-450 known as cytochrome P-448. Although induction of hepatic cytochrome P-448 regularly accompanies PCB and dioxin toxicity, cytochrome P-448 itself does not directly cause the toxicity. In investigating how receptor activation leads to the various toxic changes, it was found that the cytochrome P-448 induced by toxic PCBs and dioxins increases the metabolism of arachidonic acid. Current studies focus (1) on the role of arachidonic acid metabolites in producing the toxic manifestations of PCBs and dioxins including decreased cardiac contractile responsiveness to β-adrenergic agents and (2) the effects of dioxin induced changes in arachidonic metabolism on signal transduction pathways.

Dr. Sirotnak's research focuses on (1) molecular targets and other cellular biochemical determinants important to selective antitumor action of various categories of cytotoxic antimetabolites; (2) cytoplasmic membrane transport of pharmacologic agents; (3) molecular mechanisms of acquired resistance of tumor cells to antineoplastic agents; and (4) the regulation of folate and nucleoside transporter gene expression.

Folates play a crucial role in the biosynthesis of macromolecules. Access of tumor cells to exogenous plasma folate is made possible by the existence in the cytoplasmic membrane of a specific high-affinity transport system. Using c-DNA probes, the genetic regulation and molecular biology of this system are now being examined in models which constitutively over-produce or under-produce the transport protein and during induction of tumor cells to terminal maturation.

Folate and nucleoside analogs effectively accumulate in tumor cells via plasma membrane systems normally transporting natural folates and nucleosides. To understand the selective antitumor action of folate and nucleoside analogs, studies are being conducted of the properties and multiplicity of their cellular membrane transport, their interaction with enzymic and macromolecular targets, their intracellular metabolic disposition and their pharmacokinetic behavior. Mechanisms of acquired resistance in tumor cells to these antimetabolites and other cytoxic agents at the level of their cellular membrane transport metabolic disposition and enzymic targets are also studied.

Dr. Szeto's research focuses on opioid regulation of neurobehavioral activity and cardiorespiratory function in the developing fetus. Ongoing research efforts include: 1) role of various opiate receptor subtypes in modulating fetal cardiorespiratory function; 2) contribution of central and peripheral mechanisms in mediating the complex cardiorespiratory actions of morphine in the fetus; 3) possible link between opiate action on metabolism and its respiratory stimulation action in the fetus; 4) role of endogenous opioids in modulating the relationship between neurobehavioral activity and cardiorespiratory activity in the fetus. In addition, efforts are being made to describe the effects of opiates on the dynamical pattern of fetal breathing with the use of nonlinear mathematics.

Dr. Watanabe has a broad interest in various facets of organic chemistry and biochemistry, especially in the development of new chemical reactions and their application to the design of novel molecules that exhibit anticancer and/or antiviral activity, or are useful in elucidating enzyme reaction mechanisms. Many analogues of nucleic acid components (nucleosides) and the vitamin, folic acid, have been designed and synthesized, using new chemical reactions developed in Dr. Watanabe's laboratory. Some of these compounds showed potent anticancer or antiviral activity and underwent clinical studies. More recently, novel intercalating agents that bear covalent bond-forming capability have been synthesized, some of which showed potent anticancer activity and were found to be potent inhibitors of DNA topoisomerases. Dr. Watanabe plans to synthesize oligonucleotides of unnatural nucleosides (synthesized in his laboratory) with antisense base sequence, and to link them with the intercalating agents (also developed in his laboratory), to develop more selective anticancer agents.

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Physiology and Biophysics

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Research Activities

Dr. Windhager's studies are aimed at the elucidation of the mechanisms of ion and water transport by renal epithelial cells. The techniques used in Dr. Windhager's laboratory include: isolated perfused renal tubule segments, intracellular measurement of ions by ion selective electrodes, electrophysiological techniques, isolated membrane techniques, and expression of membrane proteins in *Xenopus laevis* oocytes. Current work centers on the role of cytosolic calcium ions as regulators of ion and water transport in proximal tubules and collecting ducts of the kidney.

Dr. Grafstein investigates nerve regeneration and transport of material in nerve axons. She is currently studying regeneration of goldfish optic nerve. Some of the conclusions reached in recent work are: Phosphorylation of axonally transported proteins is an important function in regeneration; block of physiological activity impairs regeneration by interfering with axonal transport of glycosylated constituents. Dr. Grafstein's laboratory uses the following techniques, among others: isotope tracer studies, electronmicroscopy, high resolution autoradiography, and 2-dimensional gel electrophoresis.

Dr. Maack's studies are directed to the elucidation of the physiology of cardiovascular hormones and their receptors, as well as the organ and cellular processing of peptide hormones and their receptors. In the past few years, the laboratory has been dedicated to the study of a novel polypeptide hormone, atrial natriuretic factor (ANF). Studies in laboratory elucidated the structure of ANF as well as the main functional actions of the hormone on the kidney and cardiovascular system. More recently, the laboratory discovered that a main class of ANF receptors in kidney and vasculature is involved in the removal of ANF from the circulation and plasma homeostasis of the hormone. Studies are presently under way on the cellular physiology of ANF binding, internalization, lysosomal hydrolysis and on the recycling of ANF receptors in cul-

tured cells. The techniques used in Dr. Maack's laboratory include studies in intact anesthetized and conscious rats, isolated perfused rat kidney, cell culture, receptor-hormone interactions, and general biochemical and physiological techniques.

Dr. Andersen is interested in the mechanisms by which ions cross membranes. His studies entail analysis of permeability characteristics of lipid bilayers, with emphasis on the physical and chemical properties of proteins which serve as channel formers. The emphasis of the present work is on structure-function studies of membrane channels using site-specific amino acid substitutions, and on covalent modification of voltage-dependent sodium channels using group specific reagents. Techniques used in Dr. Andersen's laboratory include: single channel analysis, electrophysiological measurements, physico-chemical analysis, and computer simulations.

Dr. Stephenson is interested in theoretical aspects of transport in biological systems. Much of his recent research centers on transport of water and electrolytes in epithelia and in the kidney. One group of current studies focuses on the relation of medullary concentration gradients and the osmolality of final urine in the mammalian kidney to tubular and vascular permeabilities, flows, and architecture. A second project is to develop a mathematical model of electrolyte transport in the whole kidney, which includes electrolytes (Na, K, Cl, HCO_3, H_2PO_4, H), glucose urea, protein osmotic forces, hydrostatic pressure, and electrical potential. Approaches to these problems include both computer simulation and the development and theoretical analysis of mathematical models.

Dr. Gershengorn's laboratory focuses on the understanding of hormonal regulation of cellular secretion. In particular, the stimulation of the anterior pituitary gland's secretion of thyroid-stimulating hormone and prolactin by thyrotropin-releasing hormone is under study. Research is now centered on the inositol lipid-calcium-protein kinase C pathway for signal transduction by TRH.

Dr. Pickering's main area of research is concerned with development of improved methods for the noninvasive measurement of blood pressure. First, he is using ambulatory monitoring techniques to learn more about the causes of blood pressure variability in normal and hypertensive subjects. This work has shown that most of the observed circadian rhythm of blood pressure can be accounted for by changes of activity. Second, he is analyzing the causes and origins of Korotkoff sounds with a view to the development of a new technique for blood pressure measurement.

Dr. Gardner's laboratory studies how neurons use chemical synaptic transmission to communicate with one another. He is concerned with the biophysics of synaptic transmission, as well as the properties of neuronal networks. Recent discoveries were: 1) choline activates inhibitory acetylcholine receptors of *Aplysia* buccal ganglia, and 2) dual-function excitatory-inhibitory synapses coordinate the two phases of their postsynaptic potentials by a voltage-dependent change in duration. Techniques used by Dr. Gardner include electrophysiological voltage- and patch-clamping, computer data acquisition and analysis, and artificial intelligence methods for neuronal modeling.

Dr. Kim studies the electrophysiology of pulmonary epithelium (especially the alveolar epithelial barrier). He also investigates macromolecule (albumin) transport across the alveolar epithelial barrier.

Dr. Lee investigates ionic mechanisms underlying changes in contractile force of cardiac muscle and ion transport across cardiac cell membrane. He recently demonstrated that cardiac glycosides increase cardiac muscle contractility by changing intracellular activities of sodium and calcium ions. Techniques used in Dr. Lee's labora-

tory include: isolated cardiac Purkinje fibers and intracellular recordings with ion selective electrodes (Na, H and Ca).

Dr. Palmer's research focuses on the mechanism of transepithelial Na reabsorption by tight epithelia, and the control of this process by hormones and other factors. The nature of the transport system facilitating sodium movement across the apical membrane of epithelial cells is being elucidated using the toad urinary bladder and the mammalian cortical collecting tubule as a model epithelia. Techniques used in Dr. Palmer's laboratory include: patch-clamping, current-voltage analysis, and flux ratio analysis.

Dr. Rabellino's research interests are primarily related to the study of the several cellular and molecular processes involved during the acquisition of functional competence by differentiating blood cells. In past studies he has investigated in the lymphoid, myeloid nd megakaryocytic series, the phenotypic evolution of developing marrow cells using monoclonal antibody technology and flow cytometry. Studies are in progress to investigate protein synthesis, cell DNA distribution and synthesis, as well as RNA accumulation in developing megakaryocytes. Also being studied are the expression and changes of specific protein genes throughout megakaryocytopoiesis using cDNA probes for different alpha granule proteins.

Dr. Reeves' laboratory research is directed toward studying the activity of the sodium-calcium exchange system in membrane vesicles prepared from the plasma membranes (sarcolemmas) of heart cells. The sodium-calcium exchange system is a carrier-mediated transport process which directly couples the transmembrane movement of calcium ions to the movement of sodium ions in the opposite direction. It is thought to play an important role in regulating the force of contraction of cardiac muscle. Previous work has included characterizing the stoichiometry, kinetics and regulation of this transport process. Current efforts are done to identify and purify the membrane protein responsible for this activity.

Dr. Rayson's research activities center on the investigation of the regulation of Na-K/ATPase (Na pump) in kidney cells. Recent discoveries include the finding that intracellular Na levels regulate the number of active Na-K/ATPase enzyme sites in outer medullary tubular segments of the kidney. Current research is directed at the analysis of the cellular mechanisms involved. Techniques used in Dr. Rayson's laboratory include: superfusion of tubular segments of the kidney, protein purification, pulse-chase and *in vitro* translation experiments.

Dr. Urban studies the molecular actions of general anesthetics on membrane ion channels. He is investigating the mechanisms by which anesthetics change sodium and potassium currents in nerves (squid giant axon) and which effects anesthetics have on single sodium channels (in lipid bilayer systems). Techniques used in Dr. Urban's laboratory include: voltage-clamp, electrophysiological techniques and lipid bilayers.

Dr. Weinstein is interested in the theory of solute and water transport across epithelia and developing a mathematical model of proximal tubular function using computer techniques.

Recent Publications

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Requirements and Course Offerings

Admission

Applications

For admission to the Graduate School of Medical Sciences an applicant must (1) have a baccalaureate degree or the equivalent from a college or university of recognized standing, (2) have adequate preparation in the chosen field of study, and (3) show promise of ability to pursue advanced study and research, as judged by his or her previous record.

Inquiries about graduate study should be addressed to the Associate Dean of the Graduate School of Medical Sciences, 1300 York Avenue, New York, NY 10021.

Candidates may be admitted in September, February, or July, although places in the graduate program for February and July may not be available because of prior commitments to applicants for September admission. Applicants for February or July admission should correspond directly with the respective Program Director regarding the availability of places.

Application material must be completed and returned to the Office of the Graduate School of Medical Sciences together with (1) official transcripts of records from all colleges and universities attended, (2) a statement of purpose of graduate study, and (3) two letters of recommendation from individuals in academic positions who know the applicant professionally. In addition, scores from the Graduate Record Examinations (GRE) are required to aid in the evaluation of an applicant. Application for taking the Aptitude (Verbal, Quantitative, and Analytical) Test and the Advanced Test of the GRE, must be made directly to the Educational Testing Service, Graduate Record Examinations, Box 955, Princeton, NJ 08541.

The proper Institution Code Number to use in your GRE application for the Cornell University Graduate School of Medical Sciences (New York City) is R 2119-6.

Applications for September or July admission and all credentials, including official transcripts of records from all colleges and universities attended, must be received by the deadline of **February 1.** Because GRE scores are an important part of the application it is of decided advantage to the applicant, to submit these scores by the February 1 deadline.

Applications and credentials for February admission must be received by November 1.

Application fee. A nonrefundable charge of $35 is made for filing an application for admission.

The completed application and all supporting documents are initially screened by the credentials committee of the program to which the student is applying. Applicants who are considered potentially acceptable are usually called for a personal interview. At the time of interview, after discussing his or her interests with the members of the Program, the applicant may tentatively select a major sponsor. If accepted by the Program, an application is forwarded to the Credentials Review Committee and then to the Dean for final decision. A student is formally notified of acceptance for study in the Graduate School of Medical Sciences by a letter from the Dean. An applicant accepted for admission is requested to inform the Graduate School of Medical Sciences of her or his plan to either accept or refuse the offer of admission within one month after the Dean's acceptance letter has been received.

It is the policy of Cornell University to actively support equality of educational and employment opportunity. No person shall be denied admission to any educational program or activity or be denied employment on the basis of any legally prohibited discrimination involving, but not limited to, such factors as race, color, creed, religion, national or ethnic origin, sex, age, or handicap. The University is committed to the maintenance of affirmative action programs which will assure the continuation of such equality of opportunity.

Admission policies are also in conformity with the policy of New York State in regard to the American ideal of equality of opportunity as embodied in the Education Practices Act.

Categories

An applicant is accepted by the Graduate School of Medical Sciences (1) as a degree candidate for the M.S. or Ph.D., or (2) as a provisional candidate.

Provisional candidacy provides opportunity for a prospective degree candidate, whose educational preparation is difficult to evaluate, to begin graduate studies. On the basis of the record of accomplishment in the first half of the academic year, the adviser or

Memorial Sloan-Kettering Cancer Center and Manhattan Skyline, as seen from Cornell Medical College.

temporary Special Committee of a provisional candidate may recommend to the Dean that (1) provisional candidacy be changed to degree candidacy, (2) provisional candidacy be continued for the remainder of the academic year, or (3) provisional candidacy be terminated. A maximum of one academic year in the status of provisional candidacy is permitted and credit of a maximum of one residence unit may be allowed on petition, provided there is convincing evidence that performance has been of the same quality as that required of degree candidates.

Special Students

Special students are students who are not degree candidates in either the Graduate School of Medical Sciences or the Medical College and who are given permission by the respective dean to take courses at either school. Special students must be degree candidates at other institutions and the courses taken at Cornell must be essential to their degree programs and are not offered by the institutions at which they are matriculated as degree candidates as certified by the institutions. Enrollment as a special student is not intended as preparation for admission to degree programs at Cornell or elsewhere.

In the case of the Graduate School of Medical Sciences, special students are accepted only with the approval of the appropriate Program Director. Special students must demonstrate special qualifications in terms of preparation and ability. They must register with the Graduate School of Medical Sciences or in the Medical College and must pay all tuition and fees before being permitted to attend lectures or laboratory sessions. Tuition is computed on the basis of the ratio of course hours taken to the total hours of instruction for the academic year (33 weeks of 40 hours). There is a registration fee of $35.

Degree Requirements

Major and Minor Programs

A candidate for the degree of Master of Science is required to register for study in one major and one minor program. Each program decides whether the Special Committee of a candidate for the Ph.D. degree must have two or three programs represented. Accordingly, a candidate for the degree of Doctor of Philosophy is required to register for study in one major and one or two minor programs. At least one of the minors must be outside the area of the major program.

The Special Committee

The general degree requirements of the Graduate School of Medical Sciences are minimal in order to give maximum flexibility in choosing a desirable program of study. The student's program is determined with the aid and direction of a Special Committee, consisting of at least three faculty members chosen by the student from those programs that best fit his or her areas of interest. Satisfactory progress toward a degree is judged by the committee rather than by arbitrary standards imposed by the Graduate School of Medical Sciences. There are no regulations of the Faculty of the Graduate School of Medical Sciences governing the specific content of instruction, courses, or grades to which the Special Committee must subscribe, except those imposed by the programs. The committee is primarily responsible for the candidate's development as an independent scholar and scientist.

No later than four weeks after enrollment, a candidate must file a statement of the major and minor programs elected for study, after which the student must choose faculty members to represent the programs and to serve on a Special Committee. The major sponsor usually advises the student concerning the other selections and chairs the committee. At least one member of the committee must represent a program different from the candidate's major program. Members may agree to serve temporarily during the candidate's first year of residence until the candidate has had the opportunity to become acquainted with areas of research in the programs of his or her choice. On completion of this year of residence, a permanent Special Committee will be formed, the membership of which can be changed with agreement of all members of the old and newly formed committees and the approval of the Dean. The members of the Special Committee decide on the student's program of study and research. They judge whether progress toward a degree is satisfactory and prepare term reports on the candidate for submission to the Dean. The members of the committee serve on all the candidate's examining committees and they approve his or her thesis.

Registration and Course Grades

No student in the Graduate School of Medical Sciences may double-register for an advanced general or professional degree with any other school or college except the Cornell University Medical College.

At the beginning of each term, students are required to register with the Office of the Graduate School of Medical Sciences and to file a registration of courses form indicating all courses they will take. A fee of $10 is charged for late registration.

At the beginning of each course in which the student is enrolling, the student will complete a separate course registration form for the instructor. All courses for which the student registers for credit will be entered in the official record. Grades of graduate students are reported as: Excellent (E), Satisfactory (S), Unsatisfactory (U), Incomplete (I), Absent (Abs.), or Unofficially Withdrawn (W). A grade of Incomplete or Absent cannot be changed later than one term following the one in which the course was taken.

Registration for the summer is required of graduate students who will be engaged in research.

Residence

The Faculty of the Graduate School of Medical Sciences regards study in residence as essential. Each candidate for an advanced general degree is expected to complete the residence requirements with reasonable continuity. A student must register each term from the time of his or her first registration in the Graduate School of Medical Sciences until the student either withdraws or completes a degree (unless a leave of absence has been granted). Full-time study for one-half academic year with satisfactory accomplishment constitutes one residence unit. Two units of residence are the minimal requirement for the master's degree and six units are the minimum for the doctoral degree. However, the time necessary to obtain the degree generally exceeds the minimal requirements. A candidate for the Ph.D. degree must spend two of the last four units of required residence in successive terms on the New York City or the Ithaca campus of Cornell University. No more than seven years may intervene between the time of first registration and the completion of all requirements for the doctoral degree. A student must complete all requirements for the master's degree in four years.

Part-time graduate study, if it is necessitated by off-campus employment noncontributory to the major program of study, is not encouraged. Requests for part-time study must be reviewed by the Executive Committee. If permission is granted for part-time study, the student must be in residence at least half-time.

Transfer of Residence Credit

No residence credit will be granted for study outside the Graduate School of Medical Sciences to fulfill the requirements of the M.S. degree. No commitment can be made about granting residence credit toward the Ph.D. requirements for previous study in another graduate school until after the candidate has entered into residence at the Graduate School of Medical Sciences. At that time, the student's Special Committee may recommend acceptance of study outside the Graduate School of Medical Sciences to the Executive Committee, which will determine the number of residence units to be awarded. No credit can be transferred for study undertaken as an undergraduate or as a special student even in courses designed for graduate students.

A student who has satisfactorily completed two or more academic years of study toward the degree of M.D. at the Cornell University Medical College, or another accredited medical school in the United States with a curriculum equivalent to that of the Cornell University Medical College, may transfer a maximum of two units of residence credit after passing an evaluation examination administered by a committee appointed by the Executive Committee of the Graduate School of Medical Sciences.

Summer Research

Registration is required for the summer research term whether or not this effort will be credited toward residence unit accumulation. Students registered for summer research pay prorated tuition only if they are obtaining residence credit. However, no degree candidate is eligible for more than two residence units in any period of twelve consecutive months.

Study *In Absentia*

A candidate for the degree of Doctor of Philosophy may petition for permission to earn residence units for study away from Cornell University while regularly registered in the Graduate School of Medical Sciences. A candi-

date to whom this privilege has been granted, must register as a Candidate *in absentia* and may work temporarily under the immediate supervision of an individual designated by his or her Special Committee although the candidate's program will continue to be directed by the Committee. For study *in absentia*, not more than two residence units may be earned toward fulfillment of the minimal residence requirements for the Ph.D. degree.

Leave of Absence

A candidate who finds it necessary to interrupt the continuity of his or her residence must petition the Dean for an official leave of absence. This written petition must specify the term of absence, state the reason for the requested leave of absence, and be approved by the student's Special Committee.

Candidacy for Degree Only

A graduate student who has fulfilled all degree requirements, with the possible exception of the thesis defense and final thesis submission, who leaves campus and is no longer a full-time student, must request Candidate for Degree Only status, which is in effect until graduation.

Examinations

Three examinations are required by the Faculty of the Graduate School of Medical Sciences: (1) Final Examination for the M.S. degree, (2) Examination for Admission to Doctoral Candidacy, and (3) Final Examination for the Ph.D. degree. Examinations are administered by an Examining Committee consisting of a chairperson appointed by the Dean, the members of the candidate's Special Committee, and, in the case of the Admission to Doctoral Candidacy Examination, one additional member selected from the Faculty of the Graduate School of Medical Sciences or of other institutions. In addition to these examinations, the candidate's major program may require a qualifying examination as part of its evaluation of the candidate after two units of residence have been completed.

For the M.S. degree: The Final Examination may be oral or both oral and written.

For the Ph.D. degree: The Admission to Doctoral Candidacy Examination is both oral and written and certifies that the student is eligible to present a thesis to the Faculty of the Graduate School of Medical Sciences. The examination should be taken after course work is largely finished but before significant thesis research has begun. Accordingly, the usual examination time will be at the end of the second year of residence. The examination may not be taken until two units of residence credit have been accumulated and a minimum of two units of residence credit is required after passing this examination before the final examination can be scheduled. The final examination for the Ph.D. degree is an oral defense of the candidate's thesis. It must be passed within four years after completion of the required residence units, or within seven years from the date of first registration, whichever is earlier.

Thesis

A principal requirement for both the M.S. and the Ph.D. degrees is the presentation of a thesis constituting an imaginative contribution to knowledge. Ordinarily, the thesis is written on a research topic in the candidate's major field of study, under the direction of the chairperson of his or her Special Committee. The time between the thesis defense and submission of the thesis in its final form is limited to 60 days. The faculty requires that the Ph.D. thesis be published in abstract and be recorded on microfilm.

Tuition and Fees

Tuition

Tuition for a student regularly matriculated in the Graduate School of Medical Sciences is $12,850 for the academic year 1989–90 and is payable in two equal parts, the first of which is due at initial registration. Tuition includes fees for matriculation, the student health plan, graduation, and miscellaneous thesis expenses.

Students in the Ph.D.-M.D. program (see p. 0) will be charged Medical College tuition ($18,100 per annum) while they are enrolled in medical school.

A student who is to receive partial residence credit (see p. 55) because of employment should apply for proration of tuition on forms obtainable at the Office of the Dean.

Other Fees

In Absentia A student registered *in absentia* pays a fee of $200 each term.

Leave of Absence Students on leave of absence will be required to pay an active-file fee of $200 for each semester, up to a maximum

of six semesters, during which they are not registered with the Graduate School. This fee will not be subject to finance charges but must be paid before the student can receive an advanced degree. Petition for waiver of this fee will be considered for students who have not completed the required number of residence units.

For students on leave of absence, the student health plan will remain in force for 30 days following the commencement of the leave.

Candidacy for Degree Only A student who registers as a Candidate for Degree Only pays a one-time fee of $35.

Any individual who owes money to the University will not be allowed to register or reregister in the University, receive a transcript of his or her record, have his or her academic credits certified, be granted a leave of absence, have a degree conferred and will not be eligible for health services and subsidized housing.

The amount, time, and manner of payment of tuition, fees, or other charges may be changed at any time without notice.

Refunds

Part of the *personally* paid tuition will be refunded if the student obtains official certification of leave of absence or withdrawal from the Graduate School of Medical Sciences during the semester. Students who terminate their registration during a regular term in this manner will be charged tuition from the registration day to the effective date of the certificate as follows: first week, 10 percent; second week, 20 percent; third week, 30 percent; fourth week, 40 percent; fifth week, 60 percent; sixth week, 80 percent; seventh week, 100 percent. No charge will be made if the effective date of leave or withdrawal is within the first six days of the term, including registration day.

Financial Assistance

All applicants to the Graduate School are requested to submit a Graduate and Professional School Financial Aid Service (GAPSFAS) form providing an estimate of financial need. The information will be used in two ways: The number of students with documentable need will allow the University to obtain maximum federal funding for loans and work-study purposes, and the specific need of an applicant *may* be used to determine that individual's graduate support. Please obtain the necessary form, available at your college or university financial aid office and from the Educational Testing Service. File the form with the Educational Testing Service, Box 2614, Princeton, New Jersey 08541, and request that the information be sent to Cornell-Code 2267.

Financial assistance is available to qualified applicants. Individual fields may offer predoctoral research fellowships, research assistantships, or teaching assistantships. These positions may provide a stipend in addition to tuition. Information about these positions may be obtained directly from the Program Director at the time of application.

Nationwide competitive predoctoral fellowships are available from the National Science Foundation and the National Research Council. Information about these fellowships should be requested directly from the appropriate governmental agency.

New York State residents are eligible for several predoctoral fellowships and the Tuition Assistance Program, which assists in tuition payments. Application forms may be obtained from the New York Higher Education Services Corporation, Student Financial Aid Section, Tower Building, Empire State Plaza, Albany, NY 12255.

Several loan programs are available to graduate students. Under these programs, repayment of the principal amount of the loan together with the interest on the loan may be deferred until after graduation. Complete information regarding loan programs may be obtained from the Graduate School Office.

Opportunity for part-time employment is often available in departmental research projects or other activities. Applications should be made directly to individual departments.

The Graduate School of Medical Sciences participates in the Work-Study Program of Cornell University which provides a significant salary contribution for qualified employed students.

Scholarships and Fellowships

Full fellowships are available for graduate students. Recipients of this award become Ph.D. Fellows and will receive a full tuition scholarship and a stipend covering living expenses.

Tuition scholarships are available for students who are not covered by a fellowship.

This scholarship fund is administered by the Office of the Dean of the Graduate School of Medical Sciences.

In addition, the following named funds provide support for selected students:

The Vincent Astor Scholarship Fund. Funds for tuition assistance are also derived from the income from a generous gift by the Vincent Astor Foundation to the Graduate School of Medical Sciences and to the Medical College. Allocation of these funds for graduate student tuition assistance is made at the discretion of the Dean of the Graduate School of Medical Sciences.

The Harry E. Gould, Sr., Medical and Graduate Student Scholarship. This fund was established by Mr. Gould's son, Harry E. Gould, Jr., in memory of his father, a prominent business and civic leader in the City of New York, who had a long-standing interest in medicine. The income from this endowment provides financial assistance for students of the Medical College and Graduate School of Medical Sciences.

The Mildred and Emil Holland Scholarship. Income from a gift by the Emil and Mildred Holland Philanthropic Fund of the Jewish Communal Fund is used to provide tuition support for an M.D.-Ph.D. student.

The Frank L. Horsfall, Jr. Fellowships are derived from income generated by the Frank L. Horsfall, Jr. Fund and are awarded each year to two outstanding students sponsored by faculty members of the Sloan-Kettering Institute.

The W. A. Keck Foundation Medical Scientist Fellowship. This award is derived from a generous endowment awarded to Cornell University Medical College and provides support for an M.D.-Ph.D. student.

The Francis L. Loeb Medical Scientist Fellowships. These fellowships have been endowed by a gift from Francis L. Loeb and provide support for two M.D.-Ph.D. students at the Cornell University Medical College.

The Shirley L. Marshak Fellowship is funded by income derived from the Shirley L. Marshak Trust for Charities. The Fellowship has been designated for award to a student of the Graduate School of Medical Sciences who is engaged in biomedical research.

The Frank R. and Blanche A. Mowrer Memorial Fund. Financial assistance is available from the income of this fund to one student each year enrolled in the Ph.D.-M.D. or M.D.-Ph.D. program.

The Papanicolaou Medical Scientist Fellowship is funded by income from a bequest from Mary G. Papanicolaou in memory of her husband, Dr. George N. Papanicolaou, and by a gift from an anonymous donor to the Cornell University Medical College. The funds provide support for an M.D.-Ph.D. student.

The Abby Rockefeller Mauzé Medical Scientist Fellowship was established by a gift from the Abby Rockefeller Mauzé Trust. The income provides fellowship support for an M.D.-Ph.D. student.

The Surdna Foundation Medical Scientist Fellowship was made possible by a generous grant to the Medical College by the Surdna Foundation. The income from this endowment provides fellowship support for an M.D.-Ph.D. student.

The Iris L. and Leverett S. Woodworth Medical Scientist Fellowship. Funds for the support of an M.D.-Ph.D. student are provided by the income from a generous gift from Dr. Leverett S. Woodworth in his own name and in memory of his wife, Iris L. Woodworth.

Awards and Prizes

The Julian R. Rachele Prize. The income of a fund established by Dr. Julian R. Rachele, former Dean of the Cornell University Graduate School of Medical Sciences, provides for an annual prize to be awarded to a candidate for the Ph.D. degree for a research paper of which the candidate is the sole or the senior author.

The prize was awarded in 1989 to James DiSanto.

The Vincent duVigneaud Prizes for the presentation of outstanding papers by students of the Cornell University Graduate School of Medical Sciences at the Annual Vincent duVigneaud Memorial Research Symposium.

Recipients of these awards in 1989 were James DiSanto, Lorraine Moran, Nila Patil, and David Solomon.

The Thesis Prizes are awarded to students of the Medical College Division who have presented an outstanding thesis during the academic year.

Recipients of these prizes in 1988–89 were Deborah Jenkins-Clark and Eric Lader.

Student Health Services

The student Health Plan of Cornell University Medical College provides hospitalization and major medical insurance for all registered graduate students. In addition, the Plan provides for ambulatory care at the Student Health Service of The New York Hospital-Cornell Medical Center. Physicians at the Health Service will refer students who require specialized care to clinics of the Hospital and to attending physicians of the staff.

The cost of medical services provided by the Plan are included in the tuition and fee structure announced by the Graduate School of Medical Sciences each academic year. Students will be issued Plan membership cards and will receive courtesy privileges at The New York Hospital Pharmacy.

Entering students are requested to have a physical examination, chest X-ray and laboratory tests performed by their personal physicians prior to matriculation. The hours of the Personnel Health Service and a complete statement of Plan benefits will be provided to each graduate student.

It is recommended that students purchase insurance coverage for eligible dependents who do not have other insurance available to them. Insured dependents are not eligible for care at the Student Health Service but they will be referred to appropriate members of the Hospital staff for medical treatment.

A student studying *in absentia* may continue hospitalization insurance by payment of the annual fees directly to the Student Accounting Office.

A student on leave of absence is not eligible to receive student health benefits.

Residence Halls

F. W. Olin Hall, a student residence, is at 445 East Sixty-ninth Street directly across from the Medical College entrance on York Avenue. Olin Hall contains a gymnasium, lounges, and 245 residence rooms. Each residence room is a single bedroom-study, but since two rooms share a connecting bath, they may be used as a suite for two students. The rooms are completely furnished. The student housing fee is $226 per month.

Livingston Ferrand Apartments, also located on East Sixty-ninth Street, just beyond Olin Hall, have furnished apartments of 1½, 2, 3, and 4 rooms. Cooking facilities are provided in these apartments. Housing fees begin at $290 per month (utilities not included). These apartments are available to married and upper-class students.

Jacob S. Lasdon House, an apartment residence, is located at 420 East Seventieth Street. This building contains studio, one-bedroom, and two-bedroom apartments and two squash courts. Apartments are fully furnished and include kitchens. Housing fees begin at $490 per month including utilities. Single, first-year students cannot be accommodated in this building.

The Rockefeller Scholars Residence at 504 East Sixty-third Street, operated by The Rockefeller University and the Memorial Sloan-Kettering Cancer Center, provides a limited number of studio apartments for married students of the Cornell University Graduate School of Medical Sciences. The monthly housing fee for these studios, which are fully furnished and contain kitchen facilities, is $530.

Housing in the above facilities is guaranteed for a five-year period from the time of first enrollment.

The fees listed may be changed at any time without previous notice.

Pets are not permitted in student housing.

Special Programs

Application to the Medical Scientist Training Program (M.D.-Ph.D.)

See p. 3 for a description of the program. Successful applicants must demonstrate a strong undergraduate science preparation, and an early commitment to a career combining both clinical and laboratory research. They must simultaneously satisfy the separate requirements for admission to Cornell University Medical College and to the Graduate School of Medical Sciences.

All documents must be forwarded to the *Office of Admissions, Cornell University Medical College, 445 East 69th Street, New York, NY 10021.* Telephone (212) 746-1067.

The following items are required, by November 30, for an application to be considered complete:

1. *AMCAS application.* (The personal data and academic record presented in this application are suitable for evaluation by both the medical and graduate schools.)
2. *Supplemental Information Form.* This form will be supplied when further information is requested.
3. Test Scores. MCAT scores are required; GRE scores are optional. If the GRE is taken, please instruct the Educational Testing Service to forward your scores.
4. *Personal statement.* A summary of the applicant's background, interests, and reasons for pursuing the combined program.
5. *Letters of Recommendation.*
   a. Statement by the pre-medical advisory committee or two letters from members of the undergraduate science faculty evaluating the applicant's suitability for a career in medicine.
   b. Letters by at least two faculty members evaluating the applicant's research potential.
6. *Application Fee.* After the AMCAS application is received, a check for $50 is requested to cover the application processing fee.

After screening, selected applicants to the program will be invited to visit the Cornell Medical Center and meet with members of the faculty of the medical and graduate programs. These interview visits will be coordinated by the Medical College Admissions Office.

Application to the Ph.D.-M.D. Program

Applications to this program (see p. 4 for description) are ordinarily made after the completion of the first year of study in the Graduate School of Medical Sciences, although more advanced students may be considered. The deadline for application is January 1.

To apply, the student must submit to the Office of the Dean of the Graduate School of Medical Sciences:

1. A completed application for admission with advanced standing to Cornell University Medical College (obtainable from the Medical College Admissions Office).
2. A plan of graduate study incorporating all required course work of the first two years of the Medical College curriculum and endorsed by the student's Special Committee.
3. Evidence of successful completion of at least two major medical school basic science courses (anatomical sciences, biochemistry, microbiology, pathology, pharmacology, physiology).
4. Two letters of evaluation from faculty of the Graduate School of Medical Sciences.
5. Results of the Medical College Admissions Test (MCAT).

The Office of the Dean of the Graduate School of Medical Sciences will review the student's credentials and make a recommendation to the Committee on Admissions of Cornell University Medical College. Only applicants who are found to be acceptable by this committee, after review of the application and personal interviews, can enter the Ph.D.-M.D. Program. Final decision will be made before June 1.

Students in this program must meet the following requirements before admission to the third-year clinical curriculum of the Medical College:

1. Complete all required graduate courses and the remainder of the first two years of the medical school curriculum.
2. Pass the Admission to Doctoral Candidacy Examination, required by the Graduate School of Medical Sciences.
3. Complete the dissertation research; present and successfully defend an original thesis at the final examination for the Ph.D. degree.

After satisfactory fulfillment of the required clinical rotations of the Cornell third-year medical school curriculum and of the required selectives of the fourth-year curriculum these students may receive credit for their graduate studies to satisfy the elective requirements of the fourth-year medical school curriculum and will then be recommended for award of the M.D. degree by Cornell University.

While registered as a graduate student in the Ph.D.-M.D. Program, the student is subject to the tuition schedule of the Graduate School of Medical Sciences. Upon completion of the requirements for the Ph.D. degree, the student is registered in the Medical College and is subject to its tuition schedule.

Programs of Study

Biochemistry

Graduate Program Chairman

A. Meister, Department of Biochemistry, Room E-106, Medical College, (212) 746-6402

Graduate Program Director

D. Wellner, Department of Biochemistry, Room E-219, Medical College, (212) 746-6409

Graduate instruction is offered leading to the Ph.D. degree. Within the framework of degree requirements and in consultation with the student, the course of study is planned to fit the need of the individual. Although formal course work is required, emphasis is placed on research. Research opportunities exist in various areas of biochemistry including enzymology, structure and function of proteins and nucleic acids, molecular biology, physical biochemistry, and the intermediary metabolism of amino acids, carbohydrates, nucleic acids, and lipids. Entering graduate students usually work for short periods in several of the laboratories of the faculty members of the Program before beginning their thesis research. Students are encouraged to choose challenging fundamental research problems that are on the frontiers of biochemistry.

The laboratories of the faculty members are equipped with virtually all of the instruments and facilities required for modern biochemical research; thus, graduate students are instructed in such methodology as chromatography, countercurrent distribution, radioactive and stable isotope techniques, spectrophotometry, electrophoresis, and analytical ultracentrifugation.

Students who undertake graduate study in biochemistry must have a sufficiently comprehensive background in chemistry to pursue the proposed course of study and must present evidence of knowledge of biology, general experimental physics, mathematics (including differential and integral calculus). Students may remedy deficiencies in these areas during the first year of graduate study. The Graduate Record Examination (the aptitude test and the advanced test in chemistry) is ordinarily required.

The student is required to demonstrate proficiency in one modern foreign language acceptable to the student's Special Committee. Proficiency in a computer programming language, as demonstrated by executing a meaningful program, may substitute for proficiency in a foreign language.

Courses

Biochemistry. This course is designed to provide the student with a knowledge of the fundamentals of biochemistry and an appreciation of the molecular basis of biological phenomena. There is an emphasis on the biochemical and molecular events relevant to human health and disease. The course is offered to both graduate and medical students. Topics covered include chemical and physical properties of biomolecules, enzymology, molecular biology, metabolism of carbohydrates, lipids, amino acids, purines, and pyrimidines. Graduate students in the Program in Biochemistry are required to pass this course (or its equivalent). First and second quarters, annually. Dr. Griffith, Dr. Wellner, and staff.

Biochemistry of Proteins. This is a research-oriented course which examines in detail the structure of proteins and the experimental methods available for increasing our understanding of these important macromolecules. Topics will include modern methods of protein isolation and structure determination. Also covered will be techniques for studying protein conformation and interaction with ligands such as substrates, coenzymes, and hormones. Graduate students in the Program in Biochemistry are required to pass this course (or its equivalent). Third quarter, annually. Dr. Wellner and staff.

Membrane Biochemistry. This course consists of a series of 15 lectures covering topics on structure-function relationships during membrane biogenesis and cell-cell interactions. Topics include membrane composition, membrane cell biology, physical techniques to study membrane structure, membrane receptors and stimulus-response coupling, membrane pathophysiology, thermodynamics, and the molecular aspects of membrane fluidity. These topics will be taught assuming that students have taken the first year Biochemistry course (or its equivalent). Third quarter of 1989–90. Dr. Hajjar.

Biochemistry for M.D.-Ph.D. Students. A course offered jointly by the faculties of the Medical College, Sloan-Kettering Division,

and The Rockefeller University. The course is primarily designed for M.D.-Ph.D. students, but Ph.D. and M.D. students may audit it. The course consists of a series of group seminars/tutorial sessions on protein structure and function, signal transduction, molecular biology and immunochemistry. Primary research papers will be assigned for student/faculty discussion. Participants will meet once a week during the first and second quarters. Offered annually. Dr. Tate.

Other Academic Offerings

Introduction to Research. Laboratory rotations in experimental biochemistry dealing with the isolation, synthesis, and analysis of substances of biochemical importance (enzymes, co-enzymes, various metabolites and intermediates), and study of their properties by various chemical and physical techniques. The student obtains this varied research experience by spending approximately two months in the laboratory of each of four faculty members of his or her choice. For incoming graduate students majoring in biochemistry.

Biochemistry Seminars. A seminar series in which students, faculty, and invited scientists from this and other institutions report on progress in their laboratories.

Cell Biology and Genetics

Graduate Program Co-Chairpersons

Donald A. Fischman, Cornell University Medical College, Department of Cell Biology and Anatomy, 1300 York Avenue, New York, NY 10021, (212) 746-6140

Joan Massague, Sloan-Kettering Institute, 1275 York Avenue, New York, NY 10021, (212) 639-8975

Graduate Program Co-Directors

David B. Donner, Sloan-Kettering Institute, Rockefeller Research Laboratories, Room 717B, 1275 York Avenue, New York, NY 10021, (212) 639-7874.

Paula Traktman, Cornell University Medical College, Department of Cell Biology and Anatomy, 1300 York Avenue, New York, NY 10021, (212) 746-6165

The Program of Cell Biology and Genetics offers a program of advanced study leading to the Ph.D. degree. The program is intended to prepare students for a career in basic research and teaching in cell or developmental biology, genetics, molecular biology, or related disciplines.

Course Requirements: In the first two years students are expected to complete a core curriculum of Graduate Biochemistry, Cell Biology, and Molecular Genetics. First year students also participate in a seminar designed to foster skills in literature comprehension and oral presentation. To satisfy the requirements for the Ph.D., the students also select four elective courses chosen to complement their background and develop their interests. Although the official transcript contains only pass/fail grades, students are expected to perform at a level corresponding to a B average.

Laboratory Rotations: Students rotate through three laboratories during the first year. Such rotations familiarize students with ongoing research in the Program and provide a mechanism for selection of the thesis sponsor. Written rotation reports also provide practice in the skills of presenting scientific data.

Admission to Doctoral Candidacy: The Program administers a qualifying examination before the end of the second year of residence. The specific format of the examination, which is composed of written and oral sections, is determined by the examining committee. Typically, the written examination covers three or four topics selected by the student and committee, and the oral examination centers around a brief research proposal on a topic chosen by the student and not related to the thesis project.

Courses

Advanced Cell Biology. Advanced course covering topics in membrane biology, cytoskeleton and cell motility, muscle cell biology, and aspects of nuclear structure and chromosome organization. The course includes lectures and group discussions of assigned research papers. Prerequisite: previous background in basic cell biology or course director's approval. Offered in alternate years. First and second quarters in 1989–90. Drs. Rodriguez-Boulan, Pardee and staff.

Molecular Genetics. The class focuses on key topics of molecular genetics in bacteria

and bacterial viruses, yeast, nematodes, Drosophila, mammalian cells and their viruses. Topics may include chromosome structure, transcriptional and translational regulation, genomic plasticity and elements of genetic diversity. The isolation of mutants and their analysis by recombination, complementation and the generation of suppressors are discussed in depth. The course includes an equal number of lectures and interactive small-group discussions of research papers from the current literature. Limited to 36 students. Offered every year with alternating faculties. Offered during the first and second quarters of 1989–90. Drs. Jack, Lustig and Osley.

Developmental Biology. Principles of descriptive, experimental, and molecular developmental biology are presented, using several animal systems as examples. Early development of the whole organism, and of cells, tissues, and organs are considered. Prerequisites: consent of the faculty. Limited to 15 students. Offered in alternate years; third and fourth quarters in 1990–91. Drs. Bachvarova and Bader.

Practicum in Electron Microscopy. A workshop in practical aspects of electron microscopy. Following a weekly lecture, students conduct specific protocols involved in electron microscopy. Topics covered include: tissue fixation, embedding and thin sectioning; transmission and scanning electron microscopy; shadow-casting of proteins and nucleic acids; immunocytochemistry; photography. All participants are required to complete an independent project. Prerequisite: Consent of instructors. Course requirements include the completion of an independent project paper. Limited to 10 students. Offered in 1990–91 during third and fourth quarters. Ms. Cohen-Gould, Dr. Fischman and staff.

Journal Club Seminar for first year students. This seminar is designed to give first-year students a chance to improve their skills in presenting and analyzing scientific data. Each student presents two papers during the semester. Papers are chosen by the students and approved by the instructors. Speakers generally provide a brief relevant background and then present each figure in the paper, summarizing the experimental method or assay used, the results illustrated, and the conclusions drawn. Participation by all students is encouraged during the presentation. Given jointly with the program in Molecular Biology. Annually, quarters 3 and 4, Drs. Fischman, Pardee, Sheffery and Shuman.

Graduate Student Seminar. This informal seminar is designed to improve graduate students' skills in public presentation. On a rotating basis, students prepare an oral presentation on their research or on a topic of their choice. The presentation is informally critiqued by the faculty. First through fourth quarters, annually. Dr. Chao and staff.

Cell Biology and Microscopic Anatomy. Offered by the Staff of the Program in Cell Biology and Genetics in conjunction with the Faculty of the Cornell University Medical College. This course follows a cellular and differentiative approach aimed at understanding the structure-function correlates that characterize the different tissues and organs. Selected topics are presented in lectures, small-group discussions and laboratory exercises designed to provide students with the skills to study and analyze cells and tissues. A microscope slide collection, presenting tissues and organs in a variety of physiological and developmental states, as well as correlative electron micrographs, are provided for individual study in the laboratory. Second and third quarters, annually. Drs. Pardee and Wall.

Gross Anatomy. Regional anatomy is studied principally through dissection of the human body. Supplementing this technique are prosections by instructors, tutorial group discussions, and radiographic and endoscopic demonstrations. Enrollment is limited and students should consult the staff early in order to determine the availability of places. First and second quarters, annually, Drs. Hagamen and Weber, and the staff.

Immunology

Graduate Program Chairman

Kenneth O. Lloyd, Sloan-Kettering Institute, Kettering Laboratory, 1275 York Avenue, New York, NY 10021, (212) 639-7468

Graduate Program Director

Robert W. Knowles, Sloan-Kettering Institute, Schwartz Laboratory, Room 1001, 1275 York Avenue, New York, NY 10021, (212) 639-7089

The program of study is developed for each student individually on the basis of the student's interest and prior experience. The Im-

munology Program has no fixed course requirements, but students generally take a core of formal courses offered by the graduate school in immunology, biochemistry, molecular biology, cell biology and genetics in order to complement their previous background and fulfill their own academic objectives. Participation in a graduate student seminar course is expected of all students to provide experience in oral presentation. Admission to Doctoral Candidacy at the end of the second year requires both written and oral examinations of the candidate's general understanding of immunology and related subjects which are relevant to the proposed research. However, the main focus of the graduate program in immunology is on laboratory research. Each student is required to undertake at least two minor research projects with different faculty members prior to developing a major research proposal for the doctoral thesis. This allows for laboratory experience to begin during the first year of the student's program. By the third year the doctoral candidate begins a full-time thesis project which typically takes two to three years. During this time the student will not take formal courses but will continue to participate in the other educational programs offered by the Institute. These include a wide variety of research seminars which are offered throughout the year with speakers from outside the Institute. In addition, the Immunology Program offers a series of colloquia on current topics in immunology with presentations and discussions led by Immunology faculty members.

Applicants should have a strong undergraduate background in the biological sciences, including biochemistry, molecular genetics, and microbiology and are also expected to have some undergraduate laboratory research experience. The application requires a personal statement describing the student's background and specific interest in the Immunology Program. An official transcript of the student's undergraduate record is also necessary with at least two letters from faculty members who can evaluate the academic potential of the student in a Ph.D. program in Immunology. Applicants must also submit the results of the Graduate Record Exam including the advanced test in Biology or Chemistry.

Courses

Immunology This course provides a broad introduction to the field of Immunology and the specific research interests of the faculty. It is designed for first-year graduate students and others with no formal training in Immunology. It includes an overview of the immune system, but also covers selected topics in detail.

These topics include techniques in immunology, B lymphocytes, immunoglobulins and monoclonal antibodies, T lymphocytes and T cell clones, immunogenetics of lymphocyte differentiation antigens, cell mediated immunity, T cell antigen receptors, natural cytotoxicity, macrophage and other accessory cells, lymphokines, the major histocompatibility complex genes and transplantation, HLA and disease associations, and tumor immunology. Quarters I and II, annually. Dr. Knowles and the Immunology Program Faculty.

Other Academic Offerings

Colloquia in Immunology Informal sessions are held monthly between students and senior faculty members to acquaint students with the major research programs headed by each of the faculty members of the Immunology Program.

Molecular Biology

Graduate Program Chairman

Kenneth I. Berns, Department of Microbiology, Room B-308, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, (212) 746-6505

Graduate Program Director

Elizabeth Lacy, Sloan-Kettering Institute, Rockefeller Research Laboratories, Room 917A, 1275 York Avenue, New York, NY 10021, (212) 639-8667

Admission A good background in genetics, molecular biology, chemistry, or biochemistry is required of students. Graduate Record Examination scores in both the aptitude test and an advanced test (biology, chemistry, or biochemistry, cell and molecular biology) are also required.

Course Requirements Students must complete a core sequence of Graduate Biochemistry, Molecular Genetics, Eucaryotic Gene Structure and Function, and Journal Club Seminar during their first year. In addition, students participate in the Graduate Research Seminar throughout their enrollment. To

complete the course requirements, eight additional quarter-equivalents of coursework must be taken before graduation chosen from a list of courses approved by the Curriculum Committee. This list currently includes: Nucleic Acids Enzymology, Cell Biology, Developmental Biology, Molecular Virology, Molecular Biology of Growth Control and Neoplastic Transformation, Electron Microscopy, and Immunology.

Laboratory Rotations Students are required to rotate through three laboratories. Laboratory rotations begin immediately after an intensive series of lectures by the faculty designed to familiarize students with the research underway in their laboratories. Rotation periods are: October–January, February–May, June–August. It is expected that students will have chosen their thesis mentor by the start of their second year in the program.

Admission to Doctoral Candidacy This examination will be given once a year at the end of the third quarter and consist of two parts, a uniform written exam and an oral defense of a written research proposal. The proposal cannot be in the same field as the student's thesis research. It is expected that most students will take this exam during their second year.

Special Committee A student's Special Committee will be chosen by the student in consultation with his/her mentor when the student selects a laboratory for thesis research. The function of the Special Committee is to evaluate the direction and progress of a student's thesis research and to serve as an informational resource for the student.

Curriculum Committee This committee, chaired by the Program Director and consisting of 8–10 members of the faculty, oversees all educational aspects of the program. The committee is responsible for assembling the curriculum, setting course requirements, adjudicating student applications for exemption from course requirements, and the composition and administration of the Admission-to-Candidacy Examination.

Courses

Eukaryotic Gene Structure and Function A semester-long course presenting the fundamentals of eukaryote gene structure, expression and regulation. Topics discussed include: DNA sequence organization, chromatin structure, viral and cellular RNA transcription, translation and its regulation, control of gene expression in model systems and molecular aspects of carcinogenesis. Third and fourth quarters, annually. Dr. Falck-Pedersen and staff.

Nucleic Acids Enzymology A formal course presenting the enzymological mechanisms and control of prokaryotic and eukaryotic transcription and DNA replication. Enzymes which alter DNA structure and shape are reviewed and topics in DNA repair and recombination are also covered. Graduate Biochemistry is a prerequisite. First and second quarters annually. Drs. Marians, Hurwitz, Rabkin, Holloman, and O'Donnell.

Molecular Virology A formal course in which major emphasis is placed on the basic mechanisms in the biology of all animal viruses, including RNA and DNA tumor viruses. The topics considered include virus structure and composition, assay of viruses and viral-specific products, transcription and replication of viral nucleic acids, translation of virus-specific proteins, assembly of viral particles, structural and functional alterations in viral-infected cells including transformation, pathogenesis of viral diseases, and viral genetics. Alternate years. Offered third and fourth quarters, 1988–89. Drs. Krug, Berns, and staff.

Molecular Genetics The class focuses on key topics of molecular genetics in bacteria and bacterial viruses, yeast, nematodes, Drosophila, mammalian cells and their viruses. Topics may include chromosome structure, transcriptional and translational regulation, genomic plasticity and elements of genetic diversity. The isolation of mutants and their analysis by recombination, complementation and the generation of suppressors are discussed in depth. The course includes an equal number of lectures and interactive small-group discussions of research papers from the current literature. Limited to 36 students. Offered every year with alternating faculties. Offered during the first and second quarters of 1989–90 by Drs. Jack, Lustig and Osley.

Molecular Biology of Growth Control and Neoplastic Transformation This course focuses on current efforts to understand the neoplastic cell phenotype from a molecular point of view. The effects of RNA and DNA tumor viruses on host cells are discussed, in particular the transformation and/or differentiation blocks of defined cell lineages by certain agents. The nature and enzymatic specificities of viral gene products responsible for transformation are compared

with related products of normal cellular genes. The potential interaction of such products with regulatory systems controlling cell shape, adhesiveness, motility, and mitosis are described, as well as the possible involvement of the same systems in nonviral neoplasias. A section of the course is devoted to the molecular biology and biochemistry of cell surface growth factor- and polypeptide hormone-receptors and mechanisms of signal transmission across biological membranes. At least part of the course consists of student presentations on relevant subjects. Third and fourth quarters, alternate years. (Next offered in 1989–90). Drs. Hayward, Rosen, Besmer, and staff.

Graduate Research Seminar This course represents an opportunity for all the faculty and students of the program to hear the upper-class students describe their research in formal seminar presentations. Quarters I–IV, annually. Drs. Lacy and Rosen.

Journal Club Seminar for First-Year Students This seminar is designed to give first-year students a chance to improve their skills in presenting and analyzing scientific data. Each student presents two papers during the semester. Papers are chosen by the students and approved by the instructors. Speakers generally provide a brief relevant background and then present each figure in the paper, summarizing the experimental method or assay used, the results illustrated, and the conclusions drawn. Participation by all students is encouraged during the presentation. Given jointly with the Program in Cell Biology and Genetics. Annually, third and fourth quarters, Drs. Sheffery, Shuman, Fischman, and Pardee.

Neuroscience

Graduate Program Chairman

Donald J. Reis, Department of Neurology, Cornell University Medical College, Kips Bay Building, Room KB-410, 411 E. 69th Street, New York, NY 10021, (212) 570-2900

Graduate Program Director

Gary E. Gibson, Department of Neurology, Cornell University Medical College, Burke Rehabilitation Center, 785 Mamaroneck Avenue, White Plains, NY 10605, (914) 948-0050, ext. 2291

The Program in Neuroscience provides training in the study of the nervous system. It includes the disciplines of neuroanatomy, neuroembryology, neurophysiology, neuropharmacology, neurochemistry, neuroendocrinology, molecular biology, and neuropsychology and perception. The program emphasizes a multidisciplinary approach to the study of the nervous system, based on the belief that future advances in our understanding of the nervous system will be derived from the thinking and research techniques employed by more than one discipline. Toward this end, the program of entering students is planned in consultation with several staff members, and the students are expected to spend some period of time working closely with members of the faculty whose interests are related to theirs. In addition, there are regularly scheduled seminars during which various aspects of work in process are presented and discussed. By these means, the students are afforded the broadest possible view of the program during their total training experience.

The student majoring in Neuroscience will be required to satisfy the requirements of the courses in neuroscience, statistics, and biomathematics, and two in the following areas: microscopic anatomy, physiology, biochemistry, and pharmacology. The student must also have two minors, at least one of which is outside the program. In addition, participation in the seminar program and advanced course offerings is expected. While there are no language requirements, it is suggested that the student achieve mastery of a modern foreign language or a computer programming language. The student choosing Neuroscience as a minor is required to participate in the neuroscience course and the seminar program as well as obtain any additional experience that the minor sponsor may suggest.

Applicants to the program are expected to have had adequate undergraduate training in biology, organic chemistry, physics, and mathematics. Graduate Record Examination scores are to be submitted with the application. An interview with the applicant is considered highly desirable.

Courses

Neuroscience This is the basic undergraduate medical school course and is required of all major and minor candidates in the program. It is a broadly based course and introduces the student to neuroanatomy, neurophysiology, and pertinent neurology. Fourth quarter annually. Drs. Brooks and Grafstein.

Neuroscience Seminar Current topics of neurosciences, not included or minimally covered in the Neuroscience course, are ex-

amined in detail. The course is required of all major candidates in the program. Fourth quarter annually. Drs. Brooks and Grafstein.

Neuropharmacology (see Program in Pharmacology).

Proseminar in Synaptic Physiology The physiology and biophysics of synapses are explored by reading and discussion of seminal papers in the original literature. The first half of the course examines a model synapse, the mammalian neuromuscular junction, by intracellular recording, voltage clamping, noise analysis, and patch-clamping. Topics in the second half include NMDA receptors, plasticity, and neural networks. Fourth Quarter 1989–90. Dr. Gardner.

Chemical Neuroanatomy This course is designed to orient students to understanding the chemical pathways of the brain. The course will discuss contemporary methods, major transmitter systems and when possible will consider pharmacological and pathological conditions. Neuroscience course, prerequisite. To be offered third quarter, 1989–90. Drs. Milner and Aoki.

Pharmacology

Graduate Program Co-Chairmen

Joseph R. Bertino, Sloan-Kettering Institute, Rockefeller Research Laboratories, Room 601, 1275 York Avenue, New York, NY 10021 (212) 639-5865

Walter-W. Y. Chan, Department of Pharmacology, Cornell University Medical College, Room LC-407, (212) 746-6250

Graduate Program Co-Directors

Michiko Okamoto, Department of Pharmacology, Cornell University Medical College, Room LC-519, (212) 746-6225

Francis M. Sirotnak, Unit of Developmental Therapy and Clinical Investigation, Memorial Sloan-Kettering Cancer Center, Kettering Bldg., Room K-316, (212) 639-7952

The Graduate Program in Pharmacology is jointly sponsored by faculties of the Medical College Division and Sloan-Kettering Division. This coordinated faculty provides the student with a broad spectrum of challenging research opportunities in modern pharmacology and a unified curriculum. Students admitted to this program will receive tuition scholarships and stipends.

Admission A baccalaureate degree with a strong background in the natural sciences and/or health sciences is required for admission. Graduate Record Examinations in both the aptitude test (verbal and quantitative) and the advanced test in Biology or Chemistry are also required for Ph.D. applicants. For applications to the M.D.-Ph.D. program, the results of the Medical College Admission Test are accepted in lieu of the Graduate Record Examination.

Course Requirements In the first two years students are expected to complete a core curriculum that may include: Graduate Biochemistry, Cell Biology, Physiology, Neuroscience, Graduate Pharmacology, Molecular Pharmacology, Molecular Biology, Immunology, and Graduate Seminar.

Minor Requirements and Laboratory Rotations Students are required to rotate through two or three laboratories. Until the student selects a major sponsor, the Curriculum Committee will supervise the student's graduate program. The minor requirements must be completed before the student can take the Admission to Candidacy Examination.

Admission to Doctoral Candidacy The Admission to Candidacy Examination consists of two parts: a uniform written exam and an oral defense of a written research proposal. It is expected that most students will take this exam by the end of their second year.

Special Committee A student's Special Committee will be chosen by the student and major sponsor in consultation with the Curriculum Committee after the student obtains a major sponsor for thesis research.

Courses

Introduction to Pharmacological Principles This course is designed to introduce the student to concepts unique to pharmacology. The introductory course will emphasize general concepts in receptor theory, the dose-response relationship, mechanisms of drug action and resistance, pharmacokinetics, metabolism, tolerance and dependence. All

first year graduate students in pharmacology are required to take this course, which is also open to all students in the graduate school. First quarter, annually. Dr. Pasternak and staff.

General Pharmacology This basic pharmacology course consists of lectures, demonstrations, and small group conferences. The purpose of these exercises is to teach the principles of pharmacology to second-year medical students and to graduate students. Detailed consideration is given to the parameters of drug action to provide the student with the fundamental concepts essential for the evaluation of any drug. Consequently, the scientific basis of pharmacology is emphasized. Prototype drugs, essentially considered systemically, serve to illustrate several mechanisms and parameters of drug action. Therapeutic applications are considered insofar as they illustrate principles of pharmacology or drug hazards. Second and third quarters, annually. Dr. Chan and staff.

Molecular Pharmacology Fundamental principles and mechanisms governing the effects of chemicals on living systems are examined from the viewpoint of drug-cell interactions. Several theoretical concepts are introduced including drug selectivity, dose-response relationships, and fundamental mechanisms of drug actions. Examples of receptor isolations, drug-receptor interactions, and effect or coupling along with natural and acquired resistance are also examined. Offered 1989–1990, fourth quarter. Dr. Bertino and staff.

Neuropharmacology This course presents the neuropharmacology of selected drugs and chemical substances that affect the central nervous system. Emphasis is placed on molecular mechanisms of drug actions with regard to the biochemistry and physiology of nervous tissue. These considerations include mechanisms of neurotransmitter actions, including drug actions that modify neurotransmitter actions. Several pharmacologic concepts important to understanding drug action on the nervous system are considered throughout. These include selectivity, specificity dose-response and receptor theory. Offered in 1989–90, third quarter. Dr. Okamoto and staff.

Pharmacology Research Seminar This course gives students the opportunity to hear Cornell faculty and invited scientists present their research. A question period enables students to probe the thinking of these scientists as they pursue their research projects. First through fourth quarters, 1989–90. Dr. Reidenberg.

Other Academic Offerings

Research in Pharmacology Research opportunities may be arranged throughout the year for graduate students who are not majoring in pharmacology but who want some investigative experience in the discipline. Special opportunities are offered for work on the nervous and cardiovascular systems and in biochemical and clinical aspects of pharmacology.

Journal Club This course is designed to improve graduate student's skills in public presentation. On a rotating basis, students prepare an oral presentation on a topic of their choice. The presentation is informally critiqued by the faculty. First through fourth quarters, annually; see the Program Directors for further information.

Physiology and Biophysics

Graduate Program Chairman

Erich E. Windhager, Department of Physiology and Biophysics, Room C-508, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, (212) 746-6358

Graduate Program Director

Thomas Maack, Department of Physiology and Biophysics, Room D-407, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, (212) 746-6343

Opportunities are offered toward the Ph.D. degree in several areas of physiology and biophysics. Ample space is available, and laboratories are well equipped to provide predoctoral training in a medical environment. Interested individuals are urged to contact the Program Chairman before preparing a formal application. Letters of inquiry should include a discussion of the educational background and indicate possible areas of emphasis in graduate study. There has been a tendency to encourage applications from individuals who have a probable interest in more than one of the areas of physiology represented within the program.

Applicants must have completed introductory courses in biology, inorganic and organic

chemistry, physics, and mathematics through the level of differential and integral calculus. Additional course work in these disciplines at the undergraduate level is encouraged. Applicants with otherwise exemplary records who lack certain course requirements will be considered for acceptance provided that they remedy their deficiencies while in training.

The course of study emphasizes the importance of teaching and research in the preparation and development of individuals for careers in physiology. This goal is achieved by a combination of didactic courses, seminars, and closely supervised research leading toward the preparation of a satisfactory thesis.

A special program of study will be developed for each student in consultation with his or her Special Committee. In addition to the general requirements set by the Graduate School for all programs, all candidates for the doctoral degree in physiology will be expected to meet the following requirements:

1. Evidence of a satisfactory background in neurosciences. Ordinarily, the course in neuroscience described under the Program in Neuroscience, or an equivalent course, will be taken concurrently with the course in physiology and biophysics.
2. Satisfactory completion of the course in physiology and biophysics, or an equivalent course.
3. For majors and minors in the program, a minimum of two elective courses in the program ordinarily will be required, in addition to the course in Physiology and Biophysics.

Courses

Physiology and Biophysics Lectures and conferences on body fluids, bioelectric phenomena, endocrinology and circulation. Third quarter, annually. Dr. Windhager and staff. Endocrinology is taught as an interdisci-

plinary course during two weeks (from 9 to 5) of this quarter using hours normally allocated not only to courses in physiology, but also in cell biology, and biochemistry (course coordinator: Dr. Greif).

Lectures and conferences on respiration, kidney function, acid-base regulation, and gastrointestinal function; and a weekly laboratory on selected aspects of physiology. Fourth quarter, annually. Dr. Windhager and staff.

Topics in Membrane Physiology This weekly conference is designed for Ph.D. and M.D.-Ph.D. students with a major or minor in Physiology and Biophysics. It is at a somewhat advanced level, especially in its quantitative approach to physiology. The aims of the conference are to train students in physiological concepts, to facilitate the understanding of lecture material in the Physiology and Biophysics course, and to establish close student-faculty contact. Third quarter, annually. Dr. Andersen.

Selected Topics in Kidney and Electrolyte Physiology and Pathophysiology Lectures, seminars and demonstrations. Topics include: 1) GFR, clearance concept, reabsorption and secretion of electrolytes; 2) concentrating mechanism; 3) electrophysiology of the nephron; 4) pathophysiology of potassium; 5) renal blood flow and its intrarenal distribution; 6) renal physiology in the newborn; 7) control of body fluid volume and tonicity; 8) pathology and pathophysiology of renal failure; urinary sediment; 9) radiology of the kidneys; 10) dialysis; 11) transplantation. Minimum of 8 students. Fourth quarter, annually. Drs. Maack, Windhager and staff.

Ionic Channels The course covers mathematical and experimental approaches to the topic of ion movement through single channels. Minimum of 5 students. Prerequisite: 2 years of calculus. Fourth quarter, annually. Dr. Andersen and invited lecturers.

Physiology of Cardiac Muscle The course is designed to present cellular mechanisms which are involved in the fundamental processes of excitation and contraction of cardiac muscle. Topics include: 1) action potential; 2) ion transport; 3) contractility (positive and negative inotropic effects); 4) excitation-contraction coupling; 5) arrhythmias; 6) cardiac failure. One laboratory day is planned for demonstrations of changes in action potential and twitch tension by inotropic agents. Minimum of 5 students. Prerequisites: third quarter physiology or equivalent. Fourth quarter, annually. Dr. Lee and invited lecturers.

Topics in Gastrointestinal Physiology Lectures and Seminars. Topics include: 1) functional morphology of stomach and intestine; 2) proliferation and differentiation of gastrointestinal cells; 3) motility of swell in esophagus, small intestine and colon; 4) gastric and intestinal secretion; pancreatic secretion; 5) lipid absorption; 6) intestinal absorption of calcium and vitamin D; 7) structure and function of bile acids; 8) gastrointestinal hormones. Minimum: 8 students. Fourth quarter, annually. Dr. Lipkin and invited experts in the field.

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Schubert, Edward T., Assistant Professor of Biochemistry in Pediatrics. B.S. 1949, M.S. 1952, Ph.D. 1959, Fordham University

Schwartz, Morton K., Professor of Developmental Therapy and Clinical Investigation. B.A. 1948, Lehigh University; Ph.D. 1952, Boston University

Scotto, Kathleen Weihs, Assistant Professor of Developmental Therapy and Clinical Investigation. B.S. 1977, St. John's University; Ph.D. 1983, Cornell University Graduate School of Medical Sciences

Seehzer, Jeri A., Associate Professor of Psychology in Psychiatry. B.S. 1956, New York University; M.A. 1961, Ph.D. 1962, University of Pennsylvania

Senterfit, Laurence B., Professor of Microbiology. Professor of Pathology. B.S. 1949, M.S. 1950, University of Florida; Sc.D. 1955, Johns Hopkins University

Sheffery, Michael, Assistant Professor of Molecular Biology. A.B. 1975, M.S. 1977, Ph.D. 1981, Princeton University

Sherline, Peter, Associate Professor of Medicine. A.B. and M.D. 1968, Boston University Medical School

Shuman, Stewart, Assistant Professor of Molecular Biology. B.A. 1976, Wesleyan University; M.D., Ph.D. 1983, Albert Einstein College of Medicine

Silverstein, Roy L., Clinical Assistant Professor of Medicine. B.S. 1975, Brown University; M.D. 1979, Emory University School of Medicine

Sirlin, Julio L., Professor of Cell Biology and Anatomy. D.Sc. 1953, University of Buenos Aires (Argentina)

Sirotnak, Francis M., Professor of Developmental Therapy and Clinical Investigation. B.S. 1950, University of Scranton; Ph.D. 1954, University of Maryland

Siskind, Gregory W., Professor of Medicine. B.A. 1955, Cornell University; M.D. 1959, New York University

Smith, Gerard P., Professor of Psychiatry (Behavioral Science). B.S. 1956, St. Joseph's College; M.D. 1960, University of Pennsylvania

Soffer, Richard L., Professor of Biochemistry. Professor of Medicine. B.A. 1954, Amherst College; M.D. 1958, Harvard University

Sonenberg, Martin, Professor of Cell Biology and Genetics. B.S. 1941, University of Pennsylvania; M.D. 1944, Ph.D. 1952, New York University

Staiano-Coico, Lisa, Assistant Professor of Microbiology in Surgery. B.S. 1976, Brooklyn College; Ph.D. 1981, Cornell University Graduate School of Medical Sciences

Stenzel, Kurt H., Professor of Biochemistry. Professor of Surgery. Professor of Medicine. B.S. 1954, New York University; M.D. 1958, Cornell University

Stephenson, John L., Professor of Biomathematics in Physiology and Biophysics. B.A. 1943, Harvard University; M.D. 1949, University of Illinois

Stokes, Peter E., Professor of Medicine. Professor of Psychiatry. B.S. 1958, Trinity College; M.D. 1952, Cornell University

Stutman, Osias, Professor of Immunology. B.A. 1950, Colegio Nacional Sarmiento (Argentina); M.D. 1957, Buenos Aires University Medical School (Argentina)

Sugg, John Y., Emeritus Professor of Microbiology. A.B. 1926, M.S. 1928, Ph.D. 1931, Vanderbilt University

Sussdorf, Dieter H., Associate Dean, Associate Professor of Microbiology. B.A. 1952, University of Missouri; Ph.D. 1956, University of Chicago

Szabo, Paul, Assistant Professor of Molecular Biology in Medicine. B.S. 1971, Ph.D. 1974, University of Illinois

Szeto, Hazel H., Associate Professor of Pharmacology. B.S. 1972, Indiana University; M.D. 1977, Cornell University Medical College; Ph.D. 1977, Cornell University Graduate School of Medical Sciences

Tate, Suresh S., Associate Professor of Biochemistry. B.Sc. 1958, M.Sc. 1960, University of Baroda (India); Ph.D. 1963, University of London (England)

Teintze, Martin, Assistant Professor of Cell Biology and Anatomy. B.S. 1976, California Institute of Technology; Ph.D. 1981, University of California

Teitelman, Gladys N., Associate Research Professor of Neurobiology in Neurology. Licendiada in Biology 1962, University of Buenos Aires (Argentina); Ph.D. 1971, University of Pennsylvania

Thaler, Howard T., Assistant Professor of Developmental Therapy and Clinical Investigation. B.A. 1967, University of California at Los Angeles; Ph.D. 1974, State University of New York at Buffalo

Townes-Anderson, Ellen, Assistant Professor of Physiology and Biophysics. B.A. 1968, Connecticut College; M.A. 1971, University of California at Berkeley; Ph.D. 1980, Boston University School of Medicine

Traktman, Paula, Assistant Professor of Cell Biology and Anatomy. Assistant Professor of Cell Biology and Anatomy in Microbiology. A.B. 1974, Radcliffe College, Harvard University; Ph.D. 1981, Massachusetts Institute of Technology

Udenfriend, Sidney, Adjunct Professor of Biochemistry. B.S. 1939, City College of New York; M.S. 1942, Ph.D. 1948, New York University

Urban, Bernd W., Assistant Professor of Anesthesiology. Assistant Professor of Anesthesiology in Physiology and Biophysics. Diplom der Physik (Master) 1974, University of Karlsruhe (West Germany); Ph.D. 1978, University of Cambridge (England)

Victor, Jonathan D., Associate Professor of Neurology. B.A. 1973, Harvard University; Ph.D. 1979, The Rockefeller University; M.D. 1980, Cornell University Medical College

Wall, Doris A., Associate Professor of Cell Biology and Anatomy. B.A. 1970, University of New Hampshire; Ph.D. 1975, Cornell University

Watanabe, Kyoichi A., Professor of Developmental Therapy and Clinical Investigation. Ph.D. 1963, Hokkaido University (Japan)

Weinstein, Alan M., Associate Professor of Physiology and Biophysics. Assistant Professor of Medicine. A.B. 1971, Princeton University; M.D. 1975, Harvard University

Weksler, Babette B., Professor of Medicine. B.A. 1958, Swarthmore College; M.D. 1963, Columbia University

Weksler, Marc E., Irving Sherwood Wright Professor of Geriatrics in Medicine., B.A. 1958, Swarthmore College; M.D. 1962, Columbia University

Wellner, Daniel, Associate Professor of Biochemistry. A.B. 1956, Harvard University; Ph.D. 1961, Tufts University

White, Perrin C., Associate Professor of Pediatrics. A.B. 1972, Harvard University; M.D. 1976, Harvard Medical School

Windhager, Erich E., Maxwell M. Upson Professor of Physiology and Biophysics. M.D. 1954, University of Vienna (Austria)

Wong, George Y., Assistant Professor of Developmental Therapy and Clinical Investigation. B.A. 1973, Rice University; M.A. 1975, Ph.D. 1978, Harvard University

Woods, Kenneth R., Adjunct Associate Professor of Biochemistry. B.A. 1948, Arizona State University; Ph.D. 1955, University of Minnesota

Yang, Soo Young, Associate Professor of Immunology. M.S. 1972, Minnesota State University; Ph.D. 1981, New York University

Young, Robert C., Associate Professor of Psychiatry in Neurobiology. B.A. 1969, Williams College; M.D. 1974, Cornell University

Zakim, David, Vincent Astor Distinguished Professor of Medicine. B.A. 1956, Cornell University; M.D. 1961, State University of New York Downstate Medical Center

Degree Recipients 1988–89

Doctors of Philosophy

Brock, Alice M., A.B. 1978, Smith College; M.S.H.S. 1980, Northeastern University. Cell Biology and Genetics, Professor Joel Pardee. Thesis: "Regulation of Actin Cytoskeleton Rearrangements During Dictyostelium Cell Motility and Vaccinia Virus Infection."

Clark, Deborah Jenkins, B.A. 1983, Williams College. Biochemistry, Professor Owen W. Griffith. Thesis: "Aminocarnitine and Acylaminocarnitines: Carnitine Acyltransferase Inhibitors Affecting Long-Chain Fatty Acid and Glucose Metabolism."

DiSanto, James P., B.A. 1983, Johns Hopkins University. Immunology, Professor Neal Flomenberg. Thesis: "Molecular Events in Human T Cell Activation: CD4, CD8 and the Human Lyt-3 Molecules."

Evans, Elizabeth V., B.A. 1980, Bennington College. Cell Biology and Genetics, Professor Paula Traktman. Thesis: "Molecular Genetic Analysis of a Vaccinia Virus Gene With an Essential Role in DNA Replication."

Groden, Joanna L., B.A. 1978, Middlebury College. Cell Biology and Genetics, Professor James L. German, III. Thesis: "Somatic Recombination in Bloom's Syndrome Cells."

Hume, Clifford Robert, B.A. 1983, Carleton College. Immunology, Professor Janet Lee. Thesis: "Regulation of HLA Class II Expression."

Kanter, Madge R., B.A. 1982, University of California at Santa Cruz. Molecular Biology, Professor William A. Hayward. Thesis: "Rapid Induction of B-Cell Lymphomas: Insertional Activation of the c-*myb* Proto-oncogene."

Lader, Eric S., B.S. 1981, Brooklyn College. Cell Biology and Genetics, Professor Dorothea Bennett. Thesis: "tctex-1: A Candidate Gene Family for a Mouse t Complex Distorter Locus (tcd) Responsible for Haploid Effects on Sperm Function."

Li, Luyuan, Graduate Certificate 1982, Sichuan University. Biochemistry, Professor Alton Meister. Thesis: "5-Oxoprolinase: Structure and Mechanism of Action."

Martinez, Humberto Jose, M.D. 1975, University of Zulia Medical School (Venezuela). Neurobiology and Behavior, Professor Ira Black. Thesis: "Actions of Nerve Growth Factor in Brain."

Qiu, Fei-Hua, M.D. 1979, Beijing Medical College. Molecular Biology, Professor Peter Besmer. Thesis: "Proto-oncogene c-kit: Structure and Relationship to the Transmembrane Receptor Kinases."

Rosenberg, Elizabeth Ann, B.A. 1981, Wesleyan University. Biochemistry, Professor Richard Soffer. Thesis: "Angiotensin Binding Protein: Biochemical and Immunological Characterization."

Rubino, Heidi, B.S. 1980, Muhlenberg College. Biochemistry, Professor Suresh S. Tate. Thesis: "Chemical Probing of the Conformation of the 3′-Functional Domain of Rabbit 18S rRNA in 40S Subunits, 80S Monosomes, and Polyribosomes."

Signorelli, Katherine L., B.A. 1982, Wellesley College. Molecular Biology, Professor Elizabeth Lacy. Thesis: "Characterization of an Insertional Mutation in a Line of Transgenic Mice."

Entering Students

Alroy, Iris, B.S. 1989, Tel-Aviv University. Major Immunology. Tel-Aviv, Israel.

Bai, Yidong, B.S. 1985, Fudan University; M.S. 1989, Shanghai Institute of Cell Biology, Academia Sinica. Major: Molecular Biology. Shanghai, P.R. China.

Castillo, Gonzalo, B.S. 1985, University of Concepcion, M.S. 1988, Catholic University. Major: Molecular Biology. Concepcion, Chile.

Chang, Shang-Yu, B.S. 1985, M.S., 1987, National Tsing-Hua University. Major: Molecular Biology. Taipei, R.O. China.

Cheng, Jie, B.M. 1988, Shanghai Medical University. Major: Neuroscience. Shanghai, P.R. China.

Cherry, David, B.A. 1989, Cornell University. King of Prussia, Pennsylvania.

Cho, Jae-Yong, B.S. 1988, Pusan National University. Major: Neuroscience. Pusan, South Korea.

Cong, Peijie, B.S. 1984, The Fourth Army Medical College; M.S. 1987, Institute of Radiation Medicine. Major: Molecular Biology. Beijing, P.R. China.

Dean, Kendra, B.S. 1985, Indiana University, Bloomington. Major: Molecular Biology. Brooklyn, New York. (Crawfordsville, Indiana).

du Quesnay, Michael, B.A., B.S. 1989, University of New Orleans. Major: Cell Biology & Genetics. New Orleans, Louisiana.

Ferguson, David, B.S. 1988, University of Rochester. Glens Falls, New York.

Flores-Rozas, Hernan, B.A. 1987, M.S. 1989, University of Concepcion. Major: Molecular Biology. Santiago, Chile.

Ghosh, Rita, B.S. 1977, M.S. 1980, Delhi University. Major: Molecular Biology. Delhi, India.

Giarre, Marianna, B.S. 1987, M.S. 1989, University of Geneva (Switzerland). Major: Immunology. Araraquara, Brazil.

Halabi, Issam, B.S. 1987, American University of Beirut. Major: Neuroscience. Beirut, Lebanon.

Han, Jihong, B.S. 1987, M.S. 1989, Nankai University. Major: Biochemistry. Tianjin, P.R. China.

Ince, Tan, M.D. 1988, Hacettepe University of Medicine. Major: Pharmacology. Ankara, Turkey.

Kim, Karl H. S., B.S. 1989, Michigan State University. Battle Creek, Michigan.

Lee, Seong-Wook, B.S. 1985, M.S. 1987, Seoul National University. Major: Molecular Biology. Seoul, Korea.

Li, Dangsheng, B.S. 1988, University of Science and Technology of China. Major: Molecular Biology. Hefei City, P.R. China.

Li, Hailong, Li, B.S. 1987, Beijing University. Major: Pharmacology. Beijing, P.R. China.

Liu, Cheng, B.S. 1982, Peking University, M.S. 1985, Capital Institute of Medicine. Major: Molecular Biology. Beijing, P.R. China.

Liu, Min, B.S. 1985, M.S. 1988, Zhongshan University. Major: Pharmacology. Guangzhou, P.R. China.

Mathew, Anitha, B.S. 1980, M.S. 1982, University of Kerala, M.S. 1989, Long Island University. Major: Cell Biology & Genetics. Brooklyn, New York. (Kottayam, India).

Mullings, Suzanne, B.A. 1989, Hunter College. Major: Cell Biology & Genetics. Jamaica, West Indies.

Peng, Hong, B.S. 1982, M.S. 1985, Institute of Zoology, Academia Sinica. Major: Molecular Biology. Beijing, P.R. China.

Pitaressi, Tina, B.A. 1983, Rutger's University. Major: Physiology & Biophysics. Berkeley Hts., New Jersey.

Rochester, S. Craig, B.A. 1989, Washington and Jefferson College. Major: Cell Biology & Genetics. Monroeville, Pennsylvania.

Rudnicki, Julie, B.S. 1989, William Smith College. Major: Cell Biology & Genetics. Batavia, New York.

Schadlow, Valerie, B.S. 1989, Cornell University. Major: Cell Biology & Genetics. Katonah, New York.

Shen, Bin, B.S. 1988, Peking University. Major: Molecular Biology. Beijing, P.R. China.

Singhania, Swati, B.S. 1987, M.S. 1989, Delhi University. Major: Biochemistry. New Delhi, India.

Su, Ching-Tien, B.S. 1989, National Taiwan University. Major: Biochemistry. Taipei, Taiwan.

Tam, Wayne, B.A., 1988, Johns Hopkins University. Rego Park, New York.

Tu, Haicheng, B.S. 1989, Pittsburg State University. Major: Physiology & Biophysics. Shanghai, P.R. China.

Woodruff, Sarah, B.S. 1989, George Washington University. Major: Immunology. Astoria, New York.

Xue, Ninrong, M.D., M.S. 1988, Peking Union Medical College. Major: Neuroscience. Shanghai, P.R. China.

Yee, Frances, B.A. 1987, Wesleyan University. Major: Neuroscience. Corona, New York.

Zhang, Hui, M.D. 1989, Beijing Medical University. Major: Immunology. Beijing, P.R. China.

Students 1989–90

Candidates for the Degree of Doctor of Philosophy

Abraham, Dicky G., M.S. 1987, Indian Institute of Technology. Major: Cell Biology and Genetics. Bombay, India

Ahn, Jong C., B.S. 1979, Seoul National University; M.S. 1981, Korea Advanced Institute of Science and Technology. Major: Molecular Biology. Gyounggido, Korea

Arnold, James B., B.A. 1982, Columbia College. Major: Neuroscience. New York, New York

August, Avery, B.A. 1987, University of California, Los Angeles. Major: Immunology. Belize

Bannerji, Rajat, B.A. 1986, Cornell University. Major: Cell Biology and Genetics. Durgapur, India

Barnhart, Kerry M., B.S. 1983, M.S. 1985, University of Arizona. Major: Molecular Biology. Tucson, Arizona

Battleman, David, B.A. 1988, Johns Hopkins University. Major: Neuroscience. Plainview, New York

Banchwitz, Robert P., B.A. 1982, Harvard University. Major: Molecular Biology. Wilmington, Delaware

Bayer, Virginia E., B.A./B.S. 1981, University of California. Major: Neuroscience. Newport Beach, California

Becker, Murray, B.A. 1985, University of Chicago. Major: Physiology and Biophysics. Chicago, Illinois

Berg, Margaret, B.S. 1985, University of Illinois; M.S. 1987, Cornell University. Major: Cell Biology and Genetics. Chicago, Illinois

Berger, Scott B., B.A. 1983, Emory University. Major: Neuroscience. Pittsburgh, Pennsylvania

Bisaha, Joseph G., B.A. 1986, Rutgers University. Major: Cell Biology and Genetics. Perth Amboy, New Jersey

Blum, Michele D., B.A. 1986, Lafayette College. Major: Molecular Biology. Philadelphia, Pennsylvania

Bosenberg, Marcus, B.A. 1976, Cornell University. Major: Molecular Biology. Middlesex, N.J.

Bradley, Roger S., B.A. 1984, Carroll College. Major: Cell Biology and Genetics. Laurel, Montana

Brayton, Cory Flagg, B.A. 1981, Williams College; D.V.M. 1985, New York State College of Veterinary Medicine. Major: Microbiology, Immunology, and Pathology. New York, New York

Brooks, David G., B.A. 1982, University of Colorado; M.S. 1984, Michigan State University. Major: Cell Biology and Genetics. Rochester, Michigan

Buck, Regina, B.A. 1988, Hunter College. Major: Immunology. Rottweil, West Germany

Burris, Judith A. Cupp, B.S./B.A. 1987, Missouri Southern State College. Major: Immunology. Carl Junction, Missouri

Cervone, Michelle, B.A. 1987, Mount Holyoke College. Major: Molecular Biology. Queens, New York

Chen, Liu-Er, B.M. 1984, Anhui Medical University; M.S. 1987, Shanghai Institute of Materia Medica. Major: Neuroscience. Anhui, China

Cheng, Peter, M.S. 1988, Tufts University, B.A. 1986, Cornell University. Major: Pharmacology. Ottawa, Ontario (Canada)

Chiu, Chang-Fang, M.D. 1980, Taipei Medical College. Major: Cell Biology and Genetics. Taipei, Taiwan, Republic of China

Cho, Hearn, A.B. 1988, Princeton University. Akron, Ohio

Cho, Sunghee, B.S. 1979, Yonsei University. Major: Neuroscience. Jinhae, Korea

Chu, Tang-Yuan, M.D. 1983, National Defense Medical Center. Major: Molecular Biology. Taipei, Taiwan, Republic of China

Claude, Alejandro, M.S. 1987, Universidad Catholica (Chile). Major: Molecular Biology, Santiago, Chile

Crombie, Andrea R., B.A. 1981, Goucher College. Major: Molecular Biology. San Diego, California

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Dicker, Adam P., B.A. 1984, Columbia University. Major: Pharmacology. Great Neck, New York

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[2]Foxman, Brett, B.A. 1982, Boston University; M.D. 1982, Boston University School of Medicine. Major: Neuroscience. Penn Valley, Pennsylvania

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Hagler, Jeremiah, B.A. 1987, University of California at Santa Cruz. Major: Molecular Biology. Santa Cruz, California

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Hearn, Timothy J., B.S. 1983, Penn State University. Major: Neuroscience. Camp Hill, Pennsylvania

Heinrich, N. Julia, B.A. 1977, Brown University. Major: Molecular Biology. New York, New York

Hodgins, Gregory W. L., B.Sc. 1985, University of Toronto. Major: Molecular Biology. Ontario, Canada

Hong, Guangyuan, B.S. 1982, M.S. 1985, Peking University. Major: Molecular Biology. Peking, People's Republic of China

Hsu, Katharine, B.S. 1987, Stanford University; M.S. 1987, Stanford University. San Marino, California

Huang, Chin-shiou, B.S. 1982, Kaohsiung Medical College; M.S. 1984, National Tsing Hua University. Major: Biochemistry. Hsinchu, Taiwan

Huang, Hsien-Bin, B.S. 1984, M.S. 1986, National Taiwan Normal University (Taipei). Major: Biochemistry. Taipei, Taiwan, Republic of China

Huang, Jinsheng, M.B. 1986, National Taiwan University. Major: Pharmacology. Taichung, Taiwan

Huber, Louise Julie, B.S. 1985, Boston University. Major: Cell Biology and Genetics. Boston, Massachusetts

Hugh, Sungoh, B.S., 1984, Seoul National University. Major: Neuroscience. Seoul, Korea

Jen, Yale I-E., B.S. 1979, National Taiwan University, M.S. 1982, Louisiana State University. Major: Molecular Biology. Taipei, Taiwan

Johnson, Ellen L., B.A. 1983, Oberlin College. Major: Molecular Biology. Tarpon Springs, Florida

Kane, Eileen M., B.A. 1985, Hunter College. Major: Molecular Biology. New York, New York

Kenny, Mark K., B.A. 1983, Wesleyan University. Major: Molecular Biology. Chappaqua, New York

Kim, Chul Geun, B.S. 1981, Han Yang University; M.S. 1983, Seoul National University. Major: Molecular Biology. Yesan, Korea

Kornack, David R., B.S. 1983, Northern Illinois University. Major: Neuroscience. Lombard, Illinois

Künzi, Myriam S., B.A. 1984, Wellesley College. Major: Cell Biology and Genetics. Upper Malboro, Maryland

Lander, Harry, B.S. 1987, State University of New York at Stony Brook. Major: Biochemistry. Lido Beach, New York

Lee, Jin-Moo, B.A. 1985, Yale University. Major: Neuroscience. Fort Washington, Maryland

Lee, Myung Soo, M.D. 1979, M.M.S. 1980 Seoul National University (Korea). Major: Immunology. Dongdaemum-ku, Seoul, Korea

Leonard, Christopher, J., B.S. 1985, Cornell University. Major: Microbiology, Immunology, and Pathology. Rochester, New York

Li, Mingxia, B.S. 1982, Beijing Second Medical College; M.S. 1985, Chinese Academy of Medical Sciences. Major: Pharmacology. Beijing, China

Lim, Lorena C., B.S. 1979, University of the Philippines at Los Banos. Major: Molecular Biology. Laguna, Philippines.

Lisanti, Michael, P., B.A. 1985, New York University. Major: Cell Biology and Genetics. Rockaway Beach, New York

Litherland, Sally A., B.S. 1981, University of Florida; M.S. 1983 University of Florida. Major: Molecular Biology. Satellite Beach, Florida

Liu, Qing, B.S. 1986, Nankai University. Major: Biochemistry. Tianjin, China

Liu, Su, M.D. 1982, Shanghai First Medical College. Major: Molecular Biology. Hunan, China

Liu, Teddy, B.S. 1987, SUNY at Buffalo. Major: Pharmacology. Hong Kong.

Lu, Bai, B.S. 1982, East China Normal University; M.Sc. 1985, Shanghai First Medical College. Major: Neuroscience. Shanghai, People's Republic of China

Luo, Yan, B.M. 1987, Beijing Medical University. Major: Molecular Biology. Beijing, China

Maddock, Anne E., B.A. 1985, Yale University. Major: Physiology and Biophysics. Fairfield, Connecticut

Mahajan, Rohit, B.A. 1984, Swarthmore College. Major: Cell Biology and Genetics. Addis Ababa, Ethiopia

Maher, Kevin J., B.S. 1984, Manhattan College. Major: Microbiology, Immunology, and Pathology. Yonkers, New York

Mahmood, Umar, B.A. 1987, California Institute of Technology. Rockville, Maryland

Maki, Robert G., B.A. 1985, Northwestern University. Major: Cell Biology and Genetics. Omaha, Nebraska

Mandell, James W., A.B. 1984, Cornell University. Major: Neuroscience. Charlottesville, Virginia

Manley, Geoffrey, B.S. 1988, University of Kentucky. Lexington, Kentucky

Marino, Michael W., B.A. 1983, Skidmore College; M.S. 1985, University of Texas. Major: Cell Biology and Genetics. Racine, Wisconsin

Mayer, Alan, B.S. 1986, M.S. 1986, Emory University. Miami Beach, Florida

McDonald, William E., B.A. 1985, University of Florida. Major: Microbiology, Immunology, and Pathology. Jacksonville, Florida

[2]McNerney, Mary Ellen, B.S. 1977, M.S. 1983, St. John's University. Major: Pharmacology. Huntington, New York

Moncrieff, Patrice M., B.S. 1984, Boston College. Major: Cell Biology and Genetics. Park Ridge, New Jersey

Moran, Lorraine M., A.B. 1982, Mount Holyoke College; M.S. 1984, St. John's University. Major: Molecular Biology. New York, New York

Morham, Scott G., B.S. 1981, Hobart College; M.S. 1985, Texas A&M University. Major: Molecular Biology. Tarrytown, New York

Muench, Marcus O., A.S. 1983, College of Marin; B.S. 1986, University of California. Major: Cell Biology and Genetics. San Francisco, California

Murakami, Monica S., B.S. 1986, University of Maryland. Major: Molecular Biology. Yokohama, Japan

Naftzger, Clarissa, B.A. 1985, University of California at Berkeley. Major: Immunology. La Jolla, California

Nicholson, Andrew C., B.S. 1973, D.V.M. 1976, Michigan State University. Major: Microbiology, Immunology, and Pathology. Bangor, Maine

Nussenzveig, Daniel R., M.D. 1980, University of Sao Paulo. Major: Physiology and Biophysics. Sao Paulo, Brazil

O'Malley, Edward K., B.S. 1985, SUNY Stony Brook. Major: Neuroscience. New York, New York

Onel, Kenan, B.S. 1984, M.A. 1985, Yale University. Major: Neuroscience. Scarsdale, New York

Onrust, Rene, B.S. 1983, M.S. 1985, Auckland University (New Zealand). Major: Molecular Biology. Christchurch, New Zealand

Packer, Alan, B.A. 1988, Brandeis University. Major: Cell Biology and Genetics. New Hyde Park, New York

Parada, Camilo A., B.S. 1978, Licence Biology (Master of Science) 1981, Catholic University of Valparaiso (Chile). Major: Molecular Biology. White Plains, New York

Patil, Nila J., B.A. 1980, University of Buffalo. Major: Cell Biology and Genetics. Buffalo, New York

Pincus, David W., B.S. 1985, Yale University. Major: Neuroscience. Hampden, Massachusetts

Ponomareff, Gregory, B.A. 1988, University of California, San Diego. Major: Molecular Biology. Oakland, California

Prescott, John, B.S. 1985, Cornell University. Major: Molecular Biology. Minneapolis, Minnesota

[2]Przybylowski, Mark D., B.S. 1987, Rutgers University. Major: Molecular Biology. Sayreville, New Jersey

Qiu, Wei-Qiao, M.D. 1982, Peking Medical College. Major: Molecular Biology. Peking, People's Republic of China

Ramakrishna, Naren R., B.A. 1985, Johns Hopkins University. Major: Cell Biology and Genetics. Charleston, West Virginia

Rempel, Rachel E., B.Sc. 1986, University of Toronto. Major: Cell Biology and Genetics. Oxford, England

Roberts, Gretchen D., B.S. 1976, George Washington University. Major: Cell Biology and Genetics. Brooklyn, New York

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[1]in absentia
[2]leave of absence
[3]candidate for degree only

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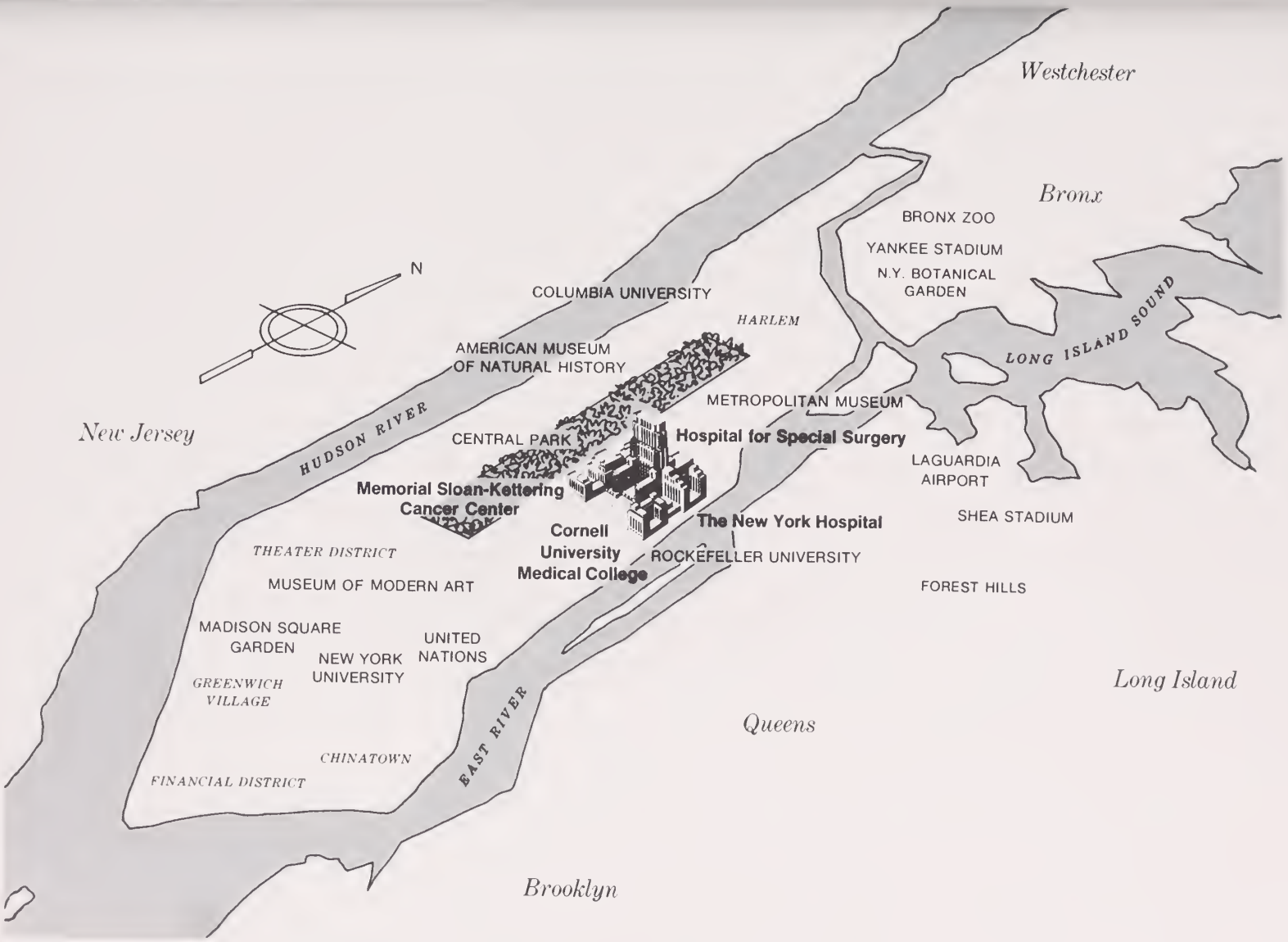
Westchester
Bronx
BRONX ZOO
YANKEE STADIUM
N.Y. BOTANICAL GARDEN
LONG ISLAND SOUND
N
COLUMBIA UNIVERSITY
HARLEM
AMERICAN MUSEUM OF NATURAL HISTORY
METROPOLITAN MUSEUM
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